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MINI-REVIEW

N-acyl homoserine lactone molecules assisted quorum sensing: effects consequences and monitoring of bacteria talking in real life

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Abstract

Bacteria utilize small signal molecules to monitor population densities. Bacteria arrange gene regulation in a method called Quorum Sensing (QS). The most widespread signalling molecules are *N*-Acyl Homoserine Lactones (AHLs/HSLs) for Gram-negative bacteria communities. QS plays significant role in the organizing of the bacterial gene that adapts to harsh environmental conditions for bacteria. It is involved in the arrangement of duties, such as biofilm formation occurrence, virulence activity of bacteria, production of antibiotics, plasmid conjugal transfer incident, pigmentation phenomenon and production of exopolysaccharide (EPS). QS obviously impacts on human health, agriculture and environment. AHL-related QS researches have been extensively studied and understood in depth for cell to cell intercommunication channel in Gram-negative bacteria. It is understood that AHL-based QS research has been extensively studied for cell-to-cell communication in Gram-negative bacteria; hence, a comprehensive study of AHLs, which are bacterial signal molecules, is required. The purpose of this review is to examine the effects of QS-mediated AHLs in many areas by looking at them from a different perspectives, such as clinic samples, food industry, aquatic life and wastewater treatment system.

Keywords Quorum sensing · AHL-related QS · Bacterial virulence · Biofilm occurrence

Introduction

Use of antibiotics and their resistance, troubles in treatment infectious diseases and Quorum sensing

Various strategies have been developed to combat pathogenic bacteria, one of the most important problems of our time. However, the progress of resistance to antibiotics makes it trouble to fight infectious diseases. This makes it necessary to discover alternative treatment methods to classical treatment ones. The discovery of the Quorum Sensing (QS) mechanism, which enables the perception of the environment in microorganisms, has gained a new perspective in the treatment of diseases (De Kievit and Iglewski 2000; Miller and Bassler 2002; Waters and Bassler 2005). By identifying the signal molecules included in the QS system of the infectious microorganism, it may be possible to separate the microorganism from fragments by initiation steps in the host at different points of binding, propagation, communication (sensing) and propagation cycle infection. This will increase the success of infection treatment.

Today, bacteria with antibiotic resistance are a serious problem worldwide. Antibiotics utilized in the treatment and recovery of infections attract attention as one of the substantial discoveries of the last century. This success against infectious agents has been overshadowed by the widespread and improper usage of antibiotics, and in consequence of the bacteria becoming resistant to antibiotics in the recent years has led to a problem that threatens public health. (Dcosta et al. 2011). Microorganisms have developed different resistance mechanisms against antibiotics to which they are sensitive, and this situation has expanded their virulence properties (Davies and Department 2010).

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Many bacterial cell–cell communication signal molecules have been found out recently, mainly, acyl homoserine lactone (AHL or HSL), hydroxyl-palmitic acid methyl ester (PAME), cyclic thiolactone (AIP), furanosylborate (AI-2) and methyl dodecenoic acid (DSF) (Derome et al. 2016). These molecules affect bacterial toxicity. Among these QS signals, AHLs are the most prominent cell–cell communication signals. The QS phenomenon is not unique to prokaryotic organisms; unicellular eukaryotic fungus pathogens also regulate their biological functions using QS signals (Albuquerque and Casadevall 2012). This communication system controls the activation of more than one mechanism in microorganisms. These bacteria develop as multicellular groups or biofilms on all living surfaces (Liu et al. 2016). In short, "QS" provides some advantages to prokaryotic microorganisms, such as the complex cell structures in eukaryotes.

In the report of the World Health Organization, it is stated that more than 60% of hospital-acquired infections have been given rise to by antibiotic-resistant bacteria (Ducel and Fabry 2002; Wilson et al. 2016). It is important to identify the agents involved in QS event for controlling diseases caused by these bacteria and to develop new treatments (Defoirdt 2018). With the usage of antibiotics in the 1930s, a unique era began for the treatment process of bacterial infections. As a result, it gave rise to a significant dropping in the number of deaths in bacterial origin infections. Nevertheless, the therapeutic methods are limited, and resistant bacteria are emerging and spreading. Naturally, the treatment of some infections has become increasingly difficult (Cámara et al. 2002).

Among the strains with the highest antibiotic resistance are Gram-negative species, including *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae* (WHO and World Health Organization 2017). Owing to multidrug resistance that develops in Gram-negative bacteria, untreatable infections may emerge recently. Most of beta-lactam antibiotics, quinolones, aminoglycosides, trimethoprim–sulfometaxozole are the basic antibiotics used in Gram-negative bacterial infections (Yekani et al. 2018). Because of the frequent use of third-generation antibiotics in prophylaxis and empirical treatment and not being included in limited antibiotic applications, the ratio of resistance to antibiotics in this group has increased (Tamma et al. 2011, 2014, 2019). Carbapenems are the most effective broad-spectrum antibiotics against Gram-negative bacilli. However, due to carbapenem resistance that develops in Gram negatives, treatment options are restricted, prolonging hospital stay and bringing along many problems, such as increased treatment costs and patient mortality (Ghafur 2014; Erdönmez et al. 2017). For example, this situation requires the addition of options, such as tigecycline and colistin to the treatment. Thus, these multidrug resistant organisms are difficult to treat and new agents are urgently needed. Nevertheless, there is no argument that this requirement could be met for foreseeable future. Gene expressions important in bacterial virulence are regulated by the QS mechanism. This situation reveals the importance of the QS system.

N-acyl homoserine lactones mediated QS

Although high living organisms use sounds and words to communicate with each other, bacteria provide this function with some communication molecules. These communication molecules are also referred to as autoinducers because of the regulation of the metabolism of the cells and other cells in which they are produced. This event is expressed as "Quorum Sensing" or environmental sensing or bacterial communication (Kravchenko et al. 2006; Khajanchi et al. 2011; Chang et al. 2014). QS is a standard mechanism utilized by the Gram-negative bacteria species and operated.

The LuxI/LuxR protein mechanism manages this kind of communication channel depicted in Fig. 1 (De Kievit and Iglewski 2000; Schauder and Bassler 2001; Turan et al. 2017). QS period begins by a LuxI protein via producing an acylated homoserin-lactone molecule. The concentration density of the produced autoinducer intensifies to an enough degree where a cognate LuxR protein perceives it and directs all dependent target genes (Schauder and Bassler 2001). Namely, LuxI-like protein is an autoinductor synthase that catalyzes the formation of a specific AHL. The AHL molecule diffuses freely across the cell membrane at high cell density. The LuxR is a transcriptional regulator system which binds to the diffusing AHL and prompts the transcription of its target genes (Li and Tian 2012).

QS is described as a communication mechanism by which a single microorganism releases the signal molecule into the medium and senses it by the population, ensuring that gene expression takes place in a coordinated manner taking into account gene expression of an entire population (Watson et al. 2002; Kawaguchi et al. 2008; Schikora et al. 2011). QS takes part an major role in the organizing of the bacterial gene that adapts to harsh environmental conditions for bacteria. It is also involved in the regulation of missions, such as formation of biofilm occurrence, bacterial virulence activity, production of antibiotic, plasmid conjugal transfer incident, pigmentation phenomenon and production of exopolysaccharide (EPS). QS directly affects on human health, environment and agriculture an overall(Turan et al. 2017). The defense process of an organism can cope with many pathogenic microbial kinds involved in virulence by QS. The coordinated invasion in the host system happens when the bacterial population density achieves sufficiently high values. The appropriate method to alleviate bacterial infections may be the control of QS signals. Bacterial actions are not advantageous

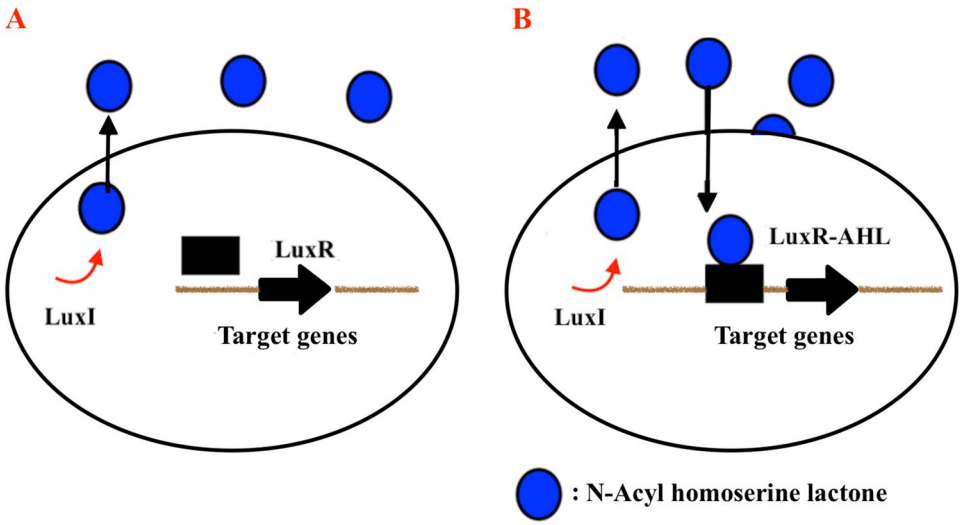

Fig. 1 The LuxI/LuxR-kind QS in Gram-negative bacteria

only when expressed by a bacterium, but may be useful to bacteria when expressed on a group basis (Kumari et al. 2008).

Many plant, animal and human pathogens compose virulence event by bacterial cell-to-cell communications through signalling molecules. The signal molecules released by Gram-negative bacteria communicate with the coordination of gene expression depending on the intensity of the bacterial population (Cataldi et al. 2007; Pinto et al. 2007; Soares and Ahmer 2011; Hou et al. 2017; Habimana et al. 2018). Bacteria communities control the existence of other bacteria by occurring and reacting to specific chemical signalling agents. There are more than one chemical signalling molecule for the communication of bacteria and these molecules are involved in the creation of the effect resulting from changes in the microenvironment by communicating both within and between species (Miller and Bassler 2002; Davis et al. 2010). It is observed that there is a difference in antibiotic resistance between the species isolated from clinical samples and the species isolated from the environment of the Gram-negative bacteria groups, such as *P. aeruginosa*, *E. coli* and *K. pneumoniae* (Cepas et al. 2019). Among the reasons for this difference, changes in microorganism metabolism due to the difference in signal molecules generated by the QS system are considered.

Many various AHL signals have been obviously identified for the last decade. The structure and concentration of AHL is extremely substantial for AHL-based QS experiments. The length of the acyl chain generally ranges from 4 to 18 carbons with increasing two carbon numbers, such as C4, C6 and C8 (Huang et al. 2016). The chemical structures with general structure of lactones are shown in Fig. 2. As seen, a lactone ring is composed of amide and carbonyl groups and one hydrocarbon chain. Although the signal molecules of *N*-acyl homoserine lactones belong to Gram-negative bacteria, oligopeptides to Gram-positive bacteria (Kumari et al. 2008).

Determining the antibiotic susceptibility of *P. aeruginosa, E. coli* and *K. pneumoniae* species isolated from various clinics and showing different resistance profiles, investigating which signal molecules are effective in infection and elucidating the relationship between the signal molecules used and resistance profiles are among the main goals in preventing the problem of resistance. It should also be aimed to investigate which signal molecules play a role in resistance to various antibiotic groups.

AHL-dependent QS researches have been comprehensively studied and understood in depth for cell-to-cell connection and communication skills in Gram-negative bacteria. The method works with three basic rules:

(i) AHL signals emitted to the environment;
(ii) an AHL synthase protein for generating the AHL signal;
(iii) the regulatory protein that senses and replies to the concentration of AHL signals (Shrout and Nerenberg 2012; Lade et al. 2014).

Screening for AHL production from bacterial strains is typically based on the bacteriological monitoring systems consisting of a phenotypic response activated via an AHL receptor protein (Ravn et al. 2001). The best studied QS system is the LuxR–LuxI system in Gram-negative bacteria with widespread antibiotic resistance, and the signal molecule is AHL. 60% of all microbial infections are caused by biofilm, the regulation mechanism of this source is done by the quorum sensing system (Jefferson 2004). The number of known QS systems is increasing day by day as various bacterial species are examined. By determining the amount and type of AHL, it will be easier to remove infections or

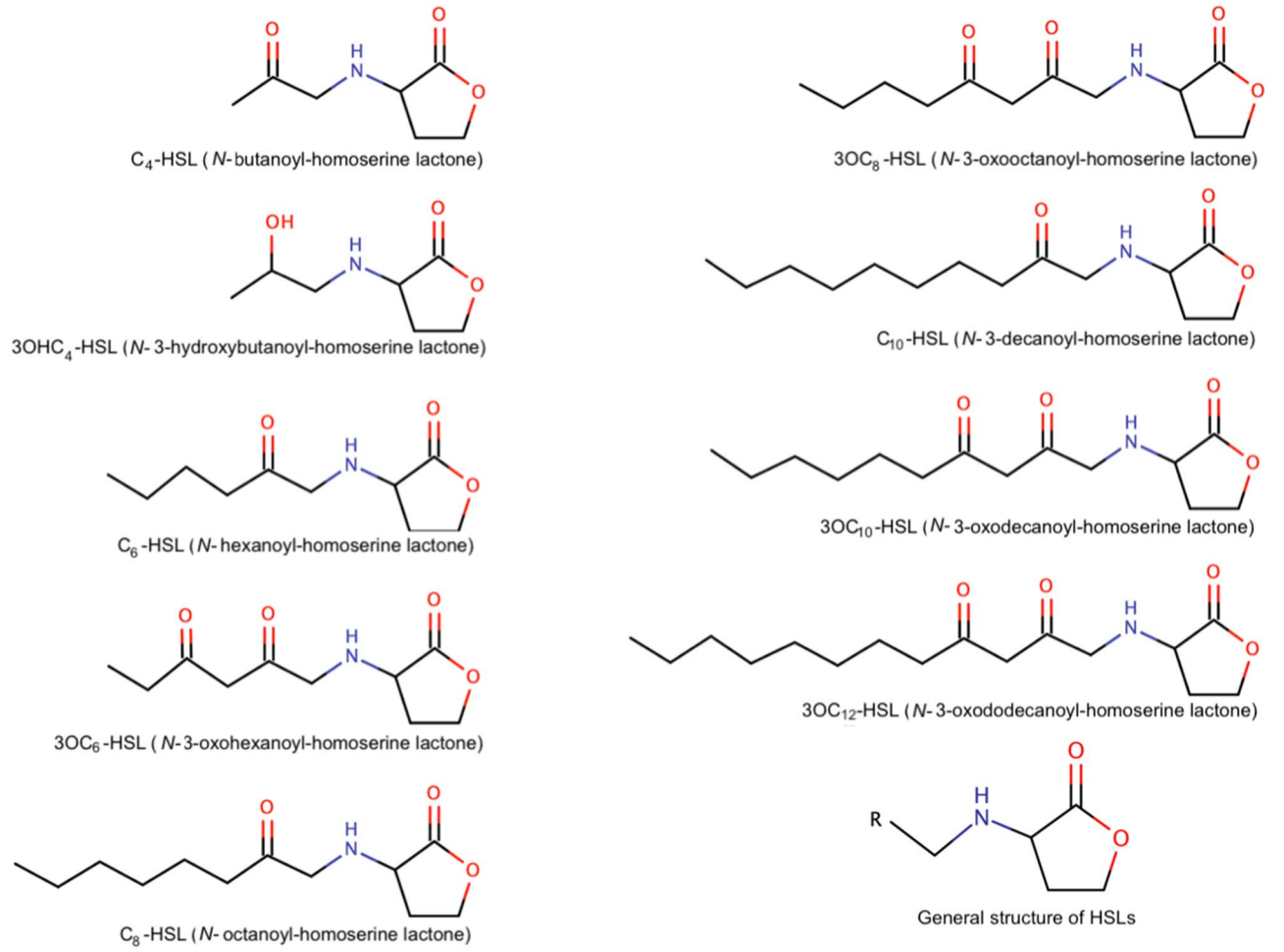

Fig. 2 The chemical structures of some HSLs with general structure

contaminated environments from the mentioned microorganisms. The detection of these AHLs in environments should not always be considered negative. For example, in a study where both nitrification and denitrification efficiencies of activated sludge systems were increased by the addition of C6-HSL and C8-HSL, it was stated that the investigation of methods to improve certain AHL-producing bacterial species would provide a potential strategy for regulation and optimization in activated sludge systems (Yan et al. 2020).

Effect, result and identification of AHLs in different areas

Diagnosing of AHLs on clinic samples

It is thought that the illumination of the bacterial communication system known as the perception of the environment or the majority, which is called the "QS" system in microorganisms, will increase the chance of success of antibacterial therapy. Therefore, the functioning of all virulence factors associated with this system will be enlightened, and its place in treatment will be revealed. It can be explained the effect of these virulence factors as follows; Due to this system, bacteria act like multicellular eukaryotic organisms and gain a number of advantages that bacteria cannot achieve alone. Many bacterial behaviors are controlled by environmental perception mechanisms. Bacteria can distinguish between low or high population densities in their environment with the signal molecules perceived by them, and thus, controlling gene expression at the population degree in response to the alteration in the number of cells in the environment.

QS is known as the language of bacteria (Turan et al. 2017). AHL, the main signalling molecules of Gram-negative bacteria can express pathogenic agents, and the QS system can take an important role in the detection of infection. AHL is significant in the organizing of bacterial virulence genes. It can also interact with eukaryotic cells, decrease an immune reply that facilitates infection (Jiang et al. 2016). Inhibition of this system, which has been found

to be effective in virulence, is a new approach in the treatment of many infections. In the formation of this inhibition, as in the action mechanisms of antibiotics, either the production of the signal molecule will be inhibited, the signal molecule will be destroyed or blocked or other bacteria will be prevented from sensing the signal molecules.

AHL based QS has also been shown to cause chronic level bacterial infections cases by *P. aeruginosa*, *B. cepacia*, which cause lung illness in patients with Cystic Fibrosis (CF) (Middleton et al. 2002; Chambers et al. 2005). QS has been represented to be managing for the formation of biofilms in both inanimate surfaces and lung tissue (Wu et al. 2000; Kjelleberg and Molin 2002; Middleton et al. 2002). Furthermore, QS acts in the pathogenesis of some gastrointestinal (GI) diseases. QS has been shown to be effective in intestinal colonization by pathogens and has been extensively proven in the regulation of virulence genes on pathogens (Sperandio et al. 1999; Surette et al. 1999; Falcão et al. 2004; Sircili et al. 2004; Kaper and Sperandio 2005; Kendall and Sperandio 2007).

Some studies have been conducted for the detection of AHL in some people based on the clinical samples. One of these studies have displayed the presence of bacterial AHL signalling molecules in sputum experimental samples of CF patients infected with *Pseudomonas aeruginosa* or *Burkholderia cepacia*. AHLs were found to check up on the expression of bacterial virulence genes. It has also been shown to be effective in triggering the occurrence of antibiotic-resistant biofilms and host chemokine releases. In this context, there are observations and evidence that different forms of inhibition of the bacterial communication system can exert antibacterial effects.

For detection of AHLs, the test samples of bronchoalveolar lavage (BAL) were experimentally determined by means of dichloromethane-extracted supernatants by utilizing the bioluminescence dependent AHL reporter plasmid pSB1075. Under these conditions, it was s observed that AHLs (C10–C14) generated light (Ward et al. 2003). These AHLs are the signalling molecules of *Pseudomonas aeruginosa*. The presence of these species of bacteria is an extensive reason of inflammation formation of the ear canal (otitis externa) in dogs. Up to this research, there has no news on finding of AHLs in the clinical samples of veterinary-related fields. Samples from ear canals with otitis externa, and samples from healthy dogs were used for controlled experiments. It enables the quantification of AHL kinds in clinical and non-clinical samples by the procedure applied. Also, a time depending diminish in AHL intensity was observed for the treated dogs. Liquid chromatography–mass spectrometry/mass spectrometry (LC–MS/MS) analytical method was conducted for defining AHLs opted *P. aeruginosa*. As a result, C4-HSL, C6-HSL and 3OC12-HSL were determined in experimental clinical samples(Kušar et al. 2016). *P. aeruginosa*, a Gram-negative bacteria, is the predominant pathogen that can infect humans and affect CF patients at certain age periods. *P. aeruginosa* infection has been reported in 60% of people with CF in the age of 16 and older in the UK. Wen et al., has been used *P. aeruginosa* AHL detection circuit to analyse CF patient sputum samples applied in an *E. coli*-based cell-free system. It was demonstared the presence of 3OC12-HSL from *P. aeruginosa*-infected respiratory samples (Wen et al. 2017). Middleton et al. have detected direct AHL in sputum samples taken from CF patients colonized with *P. aeruginosa* and *B. cepacia*. The bacterial cell detection was performed to diagnose the presence of AHL kinds. High resolution MS coupled LC was taken advantage for identification tests of AHL kinds (Middleton et al. 2002). The AHLs identified in sputum samples taken from CF patients were found as C6-HSL, 3OC12-DL-HSL. Wu et al. infected the lung tissues of mice by *P. aeruginosa* and studied experimentally (Wu et al. 2000). Bacterial detection system was used to identify AHL in in vivo experiments of these infected lung tissues. In addition, AHLs have been observed in severe pathological cases. Thus, the connection between *P. aeruginosa* and QS pathogenicity status was confirmed. Sokol et al. used a bacterial cell detection method to define AHLs in the lung homogenates of *B. kenocepacia*-infected mice (Sokol et al. 2003). Similarly, it was demonstrated the act of QS in *B. kenocepakia* infections. In another study, Jacobi et al. have studied both liver and spleen homogenates of *Y. enterocolitica* serotype O8 infected mice, which are immensely pathogenic in mice, both in vitro and in vivo (Jacobi et al. 2003) and used a bioluminescence bacterial cell detection system to detect AHLs. In this study, the relationship between QS-based AHL relationship was confirmed. The resistance of bacteria to antibiotics has been shown in Fig. 3.

The importance of AHLs in food industry

The formation of persistent biofilms containing pathogens is one of the big problems in the food processing industry, as surface contamination in contact with food can have significant public health impacts (Jamuna Bai 2016). Compounds found in food matrixes and storage conditions can affect the production of AHLs (Medina-Martinez et al. 2006). *Pseudomonas spp.*, *P. fluorescens, P. putida* and *P. fragi* are the proteinaceous dominant spoilage microbiota for aerobically cooled beef (Jay et al. 2003), raw milk (Kraft 1992), fish (Tryfinopoulou et al. 2002), chicken (Arnaut-Rollier et al. 1999) and protein products (Gennari and Dragotto 1992; Ternström et al. 1993). Other some spoilage organisms in aerobic cold manner stored raw foods are kinds of *Aeromonas, Shewanella, Moraxella, Psychrobacter* and *Acinetobacter* and psychrotrophic members of the *Enterobacteriaceae,* such as *Hafnia alvei, Serratia spp.* and *Enterobacter*

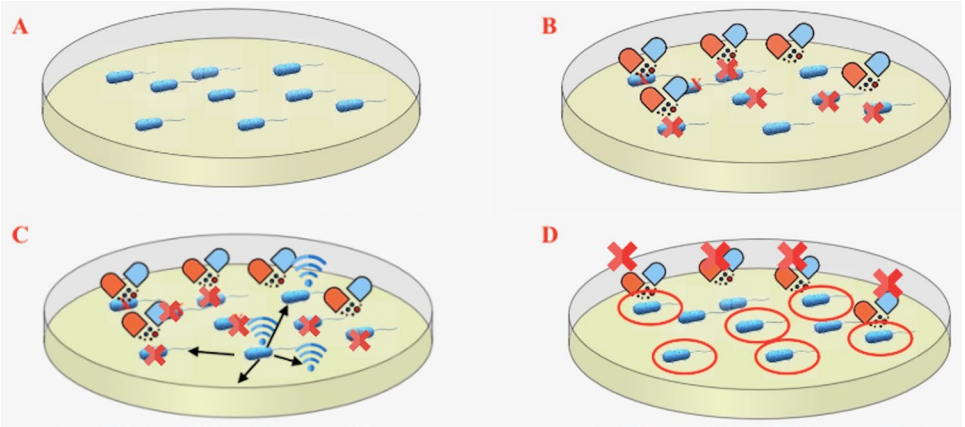

Fig. 3 The resistance of bacteria to antibiotics; **a** Bacteria medium, **b** Destruction of some bacteria with the addition of antibiotics in the environment, **c** Communication of bacteria not destruction in the environment with the help of signal molecules, **d** After signalling, bacteria provide resistance to antibiotics

spp (Borch et al. 1996; Stanbridge and Davies 1998; Liu et al. 2006). Medina et al. conducted a study to make a decision on AHL production of *A. hydrophila* and *A. caviae* strains and to appraise the effect of environmental reasons on AHL generation. It was presented that the *Aeromonas* test strains could compose AHLs (especially C4-HSL) with a different of status of temperature effect, pH, NaCl concentrations usually were come across in foods linked with this microorganism when increasing enough numbers (population density) was accessed (Medina-Martinez et al. 2006).

Meat is one of the most consumed food products and has a very short shelf life. In one study, the samples of beef were investigated for microbial relation and the existence of AHLs during the storage studies. Isolates were monitorized for AHLs formation, and opted spices were followed by QS inhibitory (QSI) activity. The impact of added spice process on AHLs manufacturing of *Y. enterocolitica* was indicated by quantitation via high-performance thin layer chromatography (HP-TLC). The results demonstrated that microbial relation of beef mostly happens in the presence of *Enterobacteriaceae* and lactic acid bacteria (LAB). Outcomes showed the asset of AHLs in beef meat during the spoilage event. It was also observed that the spice decreased the formation of AHLs by reducing the spoilage rate. (Gopu and Shetty 2016). In another study, AHLs were diagnosed from five commercially genarated vacuum-packed meat samples. It was showed that compounds stimulating QS mechanisms are prevalent in spoiling vacuum pack meat within scope of study (Bruhn et al. 2004). The schematic representation of bacterial AHL production, uptake of signal molecules by the bacterial receptor and gene expression is shown in Fig. 4.

Effect of AHL molecules on aquatic life

The seafood sector is among the fastest developing food production industry worldwide. Pathogens causing infectious diseases can cause great economic damage to the aquaculture industry. *Aeromonas spp.* and *Vibrio spp.* are the most common aquatic pathogens that kill shrimps, fish and molluscs (Niu et al. 2014; de la Fuente et al. 2015; Zhao et al. 2015; Baker-Austin and Oliver 2018). Bacteria attack these living organisms by QS-originated pathogenicity. Conventionally, bacterial infections are cured using antimicrobials. Even if there are numerous remedy methods which are accepted useful in aquaculture, the studies requiring methods that can minimize commercial economic losses on an industrial scale should be carried out (Kalia et al. 2019). Most of farmers also apply antibiotics in a prophylactic strategy, even when pathogens do not become apparent(Holmström et al. 2003). This application has concluded in the progress of (multiple) antibiotic resistance (Cabello 2006) which does antibiotic treatments impotent in inspection of diseases (Karunasagar et al. 1994; Defoirdt et al. 2011). In one of the studies, a cell sensor was developed and used to measure the QS signalling molecule. It is aimed to monitor the bacteria responsible for the degradation of freshwater fish production in real time. A cell sensor was developed and used to measure the QS signalling molecule. A modified carbon electrode is used to increase accuracy. Electrochemical impedance spectroscopy has been used to save the cell impedance signal affected by *Pseudomonas aeruginosa* and has been determined 3OC12-HSL molecules. As a result of this work, it was concluded that it could serve as an effective and innovative approach in monitoring deterioration in freshwater fish production (Jiang et al. 2018). In another study, the presence of AHLs in marine bacterial strains collected from heavily contaminated surfaces in the Gulf of Santa Marta (Colombia) has been proven. The detection and identification process of AHLs were carried out by operating the microbial biosensor *Escherichia coli* (pSB401) and GC–MS, HPLC–MS experiments. All isolated marine strains have been found to have QS systems mediated by C4-HSL or C6-HSL, and in some cases both (Cuadrado-Silva et al. 2013). AHLs act a crucial role in Gram-negative bacterial communication channel

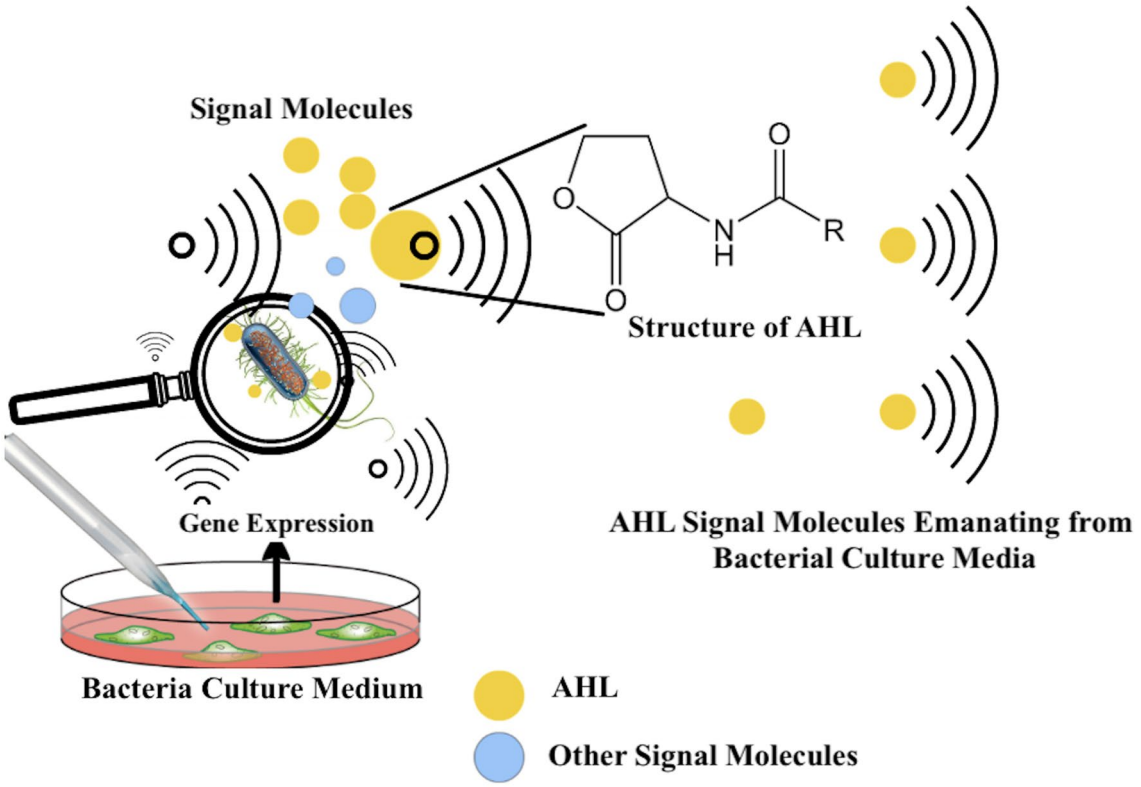

Fig. 4 Schematic representation of bacterial AHL production, uptake of signal molecules by the bacterial receptor and gene expression

by supporting the constitution of biofilms and extracellular polymeric substances (EPS). Wang et al. developed a stable and sensitive procedure for detection of AHL. To obtain AHLs and detect concentration level of AHLs in wastewater treatment biofilms ultrasonic extraction, an Oasis hydrophilic–lipophilic-balanced (HLB) sorbent system in column format assembled with ultra-performance liquid chromatography linked to tandem mass spectrometry (UPLC-MS/MS) was used. This method is ideal and easy to follow process for quantitative experiments of AHLs in wastewater treatment biofilms (Wang et al. 2017).

Sturgeon is fresh water-culture fish in China, and it has high susceptibility to spoilage. In order to identify QS signals acting on sturgeon, it was checked whether QS was involved in spoilage. Control of production of AHLs and specific spoilages were performed on sturgeon stored at 4 °C. At the end of study by thin layer chromatography (TLC), high-performance liquid chromatographytriple quadrupole tandem mass spectrometry (HPLC-TQMS) and high-performance liquid chromatography–quadrupole time-of-flight mass spectrometry (HPLC/qTOF-MS), it was assigned that the AHLs generated by *A. veronii* were C6-HSL, C8-HSL, 3-oxo-C8-HSL and 3-OH-C8-HSL. This study brought to light that QS system was probably mediated in the regulation of sturgeon spoilage. First, it was declared that the spoilage caused by *Aeromonas* was from C8-HSL and 3-OH-C8-HSL production (Gui et al. 2018).

Industrial significance of AHL molecules and their effect for wastewater treatment system

AHLs utilized by Gram-negative bacteria communities are one of the best defining signal molecules that play an important role in organizing virulence factor secretion, manufacturing of exoenzyme and QS originated biofilm formation (Ma et al. 2018). The cooling water procedures are applied to eliminate heat constituted in different industries. Biological contamination with microorganism accumulation on wet surfaces is one of the major trouble in cooling water systems. Biological contamination of these systems gives rise to blockage of condenser pipes and heat exchanger pipes. Okutsu et al. examined the event between QS and biofouling in the cooling water system. These researchers took 192 bacterial strains from the five cooling water systems and monitored for AHL formation. AHLs extract samples were made a decision as *Aeromonas hydrophila*, *Lysobacter* sp., *Methylobacterium oryzae* and *Bosea massiliensis*. AHLs formed by *B. Massiliensis* as follows: C6-HSL, 3-oxo-C6-HSL and 3-oxo-C8-HSL. AHLs occurred by *Lysobacter* sp. were

assigned as C10-HSL and 3-oxo-C10-HSL. Samples were defined with liquid chromatography–mass spectrometry (LC–MS) (Okutsu et al. 2016). The formation of AHLs in membrane bioreactors remeding wastewater has paid much attention as AHLs have been presented to play critical role in biofouling (Huang et al. 2020). AHL-mediated QS mechanisms are responsible for occurrence of biofilm, swarming motility (Labbate et al. 2004) and the formation of microbial by-products, which ensure architectural assistance for biofilms in membrane bioreactor (Tan et al. 2014). C6-HSL, C8-HSL, 3-oxo-C8-HSL, C10-HSL and C12-HSL are universally diagnosed in membrane bioreactor wastewater treatment systems (Yeon et al. 2009; Oh et al. 2012; Kim et al. 2013; Yu et al. 2016a, b, 2019; Liu et al. 2019).

Lately, QS has known significant acts in biologically wastewater treatment operations. Honda et al. studied to research the variety of AHL molecules both biological wastewater treatment procedure and their places (Honda et al. 2019). They tested and measured 10 AHLs in activated sludge samples at wastewater treatment factories. For this aim, these researchers were used Fourier transform mass spectrometry (FTMS) and bioassay on TLC. Determination of AHL via LC-FTMS was found much more responsive than TLC experiments. The sludge samples were gathered at seven wastewater treatment plants in Japan and Thailand, which were selected to check against different process kinds containing a pilot-scale membrane bioreactor procedure. As a result, they identified C4-HSL, C7-HSL and C8-HSL kinds of AHL in the samples (Honda et al. 2019). Increasing in cell density after communication of bacteria among themselves is shown in Fig. 5.

Prevention of production of quorum sensing molecules

Tatedo et al. observed in their study on *P.aeruginosa* isolates that azithromycin affects gene regions responsible for bacterial communication, thereby reducing signal molecules and preventing elastase gene expression. It has also been found that a molecule called triclosan inhibits an enzyme responsible for signal molecule synthesis (Tateda et al. 1996).

Degradation of *N*-acyl homoserine lactone signal molecule or inhibition

Degradation of the synthesized *N*-acyl homoserine lactone molecules may be another target. This mechanism is provided by either enzymes or some inhibitors. The signal molecules of Gram negatives can be destroyed by AHL lactonase and AHL acylase. The signal molecules of Gram positives can be destroyed by some inhibitors. It has been reported that phenolic inhibitors "closantel" and "RWJ-49815" disrupt protein metabolism by inhibiting histidine kinase (Zhang and Dong 2004).

Prevention of uptake of the lactone signal molecule of *N*-acyl homoserine

Blocking the synthesis of signal receptor proteins or reducing the binding of these proteins to the receptor by AHL analogs can also be applied as a separate mechanism to inhibit the reception of the majority sense signal. It has been reported that the furanone compounds produced by *Delisea pulchra*, a red macro algae and stored in its vesicles, are structurally linked to the LuxR protein, which is an AHL

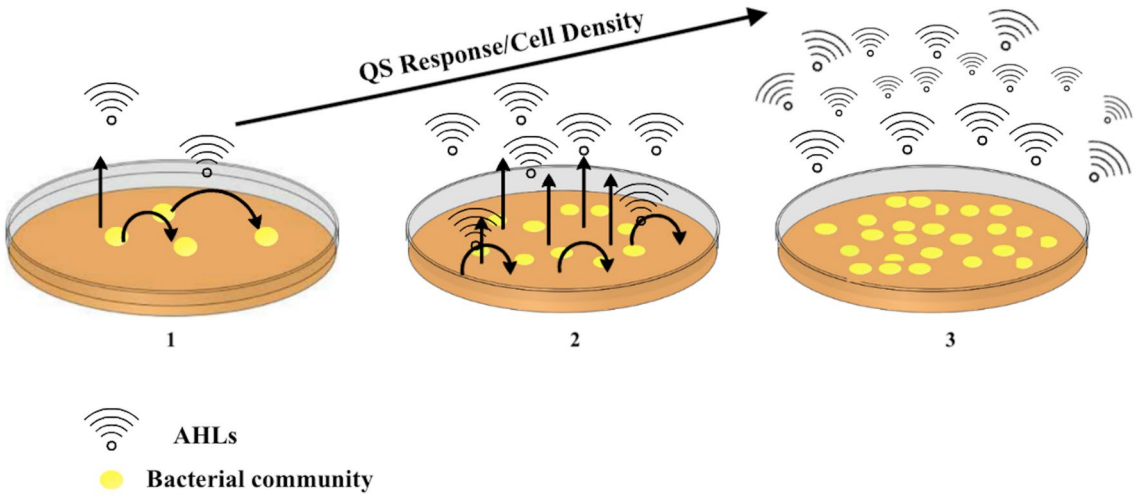

Fig. 5 Increase in cell density after communication of bacteria among themselves and with the surrounding bacteria

signal analogue, leading to the release of AHL and thus inhibiting the bacterial environment detection system of *V. fisheri* (Rasmussen and Givskov 2006).

Conclusion

Researches conducted in the past years have been provided an important perception of cell-to-cell communication and cooperation systems. AHLs in the QS systems are bacterial signal molecules. One of the most significant conditions for defining the QS system is the presence of AHLs in the environment. That's why it is extremely important to get to know AHLs. Many bacterial events can be overcome by understanding the QS system.

The recent researches have suggested that knowing the density of the QS can offer many advantages. The purpose of this review is to emphasize the importance of QS-based AHLs as QS affects health, agriculture and environment. Having knowledge of QS-mediated AHL systems are extremely critical for future studies in many areas, such as health, food, agriculture and industry. Thus, we are of the opinion that this review will attract attention in related areas.

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Authors' Contributions ÖA: conceptualization, writing review and editing. DE: conceptualization, writing review and editing. BÖA: conceptualization, writing review and editing. MO: conceptualization, writing review and editing. All the authors agreed to submit the manuscript.

Declarations

Conflict of interest statement Nothing declared.

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