Review Article

Quorum Sensing Signaling in Bacteria - from Mechanism to Future Prospects: A Terse Literature Review

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ABSTRACT

Quorum sensing is when a sufficient population of micro-organisms, such as bacteria, situated in a given environment can trigger a system of cell-cell communication in these micro-organisms. Researchers, increasingly, have shown that bacteria are unable to thrive independently as solitary cells, but as colonial organisms, communicating intercellularly, and enhancing their capacity to adapt to changing environmental conditions. To a great extent, researchers today have come to terms with the intricacies surrounding bacterial conversations, and responses/signals. Herein, the quorum sensing and its signaling in bacteria, from briefs about the mechanism, its discovery, and involved molecules, to its applications/uses has been tersely reviewed. Understanding bacteria quorum sensing mechanisms/processes can be very challenging. Several strategies employed to disrupt quorum sensing in bacteria have involved receptor inactivation, signaled synthesis inhibition including its degradation, blocking of quorum sensing using antibodies, as well as the combination of antibiotics and anti-quorum sensing agents. The future use of quorum sensing is hopeful, given the emerging applications like its use in biofouling reduction, biofuel production, biodegradation as well as winemaking.

Key words: Quorum sensing signals, Bacteria, Pathogens, Auto inducer, Inhibitors, Bio-preservatives.

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INTRODUCTION

Bacteria are organisms belonging to a group considered among the most primitive living entities. For the proper growth and development of all multicellular living organisms, signaling (cellular) and transmission in bacteria are very essential.[1] Through intercellular signaling, micro-organisms display particular behaviour that usually results in divergent gene regulation.[2] Some gram-negative and positive bacteria can organise communal behaviours, which involve certain signaling molecules, synthesized by these bacteria when they grow in their environment. Being population density-dependent, cell communication in bacteria constitutes a synthesis of, and response to the presence of auto inducers, which are biochemical in nature and considered as tiny pheromone-like molecules. When a certain critical amount of these molecules is attained, signal recognition by these bacteria indicates that enough number or "quorum" of these bacteria is now available. Accordingly, this reaction occurs through an ordered expression of some genes, which allow the bacteria to produce a combined response, thus it is one of the ways the organism ensures its population survives in the environment.[2] Such responses may include both initiating and establishing genetic competence,

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regulating their ability to cause disease/infection, and synthesis of antimicrobial peptides.[3-5]

A sufficient population of micro-organisms, such as bacteria, situated in an environment can bring about a trigger to the system, and the entire process that brings about this situation is captioned 'quorum sensing'.[6] Simply put, 'quorum' can be said to mean threshold, while 'sensing' may mean feel. Therefore, the 'quorum sensing' system portrays a cell-cell signaling mechanism that permits the bacteria to be in control of the expression of certain genes that depend on the number of cells within a given locality.[7,8] Bacteria produce some chemical messenger molecules called auto inducers (AIs) (or self-inducers used to coordinate behaviours). These molecules are first biosynthesized inside the cells and excreted out into the cell's surroundings. Soon after these molecules accumulate beyond the thresholds outside of the bacterial cell, the pathways for signaling are switched on so that the (bacterial) cells respond to the message by altering the gene expression and modulating the physiological processes.[5] Researchers have increasingly shown that bacteria would not live independently as solitary cells, but as colonial organisms, able to utilize detailed systems that communicate in intercellular pathways, to enhance their capacity to adapt to changing environmental conditions.[9] Hence, bacteria can connect one another, particularly through chemicals, which are excreted from cells that can elicit profound physiological changes.[2,5,9]

Before now, the intricacies of bacteria signals seemed alien to researchers. Today, researchers can understand, to a great extent, these intricacies of bacterial conversations, and responses/signals.[10] Much of this has been made possible due to research advancements in molecular biology alongside innovative technologies that rapidly enhanced the understanding of quorum-sensing.[3,9] By understanding the mechanism by which cellular communication is carried out in bacteria, there could be the formation of a strong foundation for the development of techniques to help block these signaling systems and thereby control the activities of bacteria in the environment, for example, in their ability to cause disease/infection[11] and probably in the bacterial spoilage of food. Additionally, the enlarging worldwide distribution of crop plants has put an additional impetus in looking for new ways of increasing the production and improving the ability of crop plants to resist disease and extending their shelf-life.[12] In this context, therefore, this terse review seeks to reiterate the import of quorum sensing and signaling in bacteria; from its discovery, understanding the mechanism process and involved molecules, to its possible applications/uses.

SURVEY METHODOLOGY

The first step in conducting this current terse review was to formulate the research question, which helped us ascertain the research area/field to focus on, bearing in mind the target audience that would be interested in this article. The next step was the search strategy, which would elaborate the literature search for published papers on 'quorum sensing and or signaling' together with 'bacteria'. Based on this topic, search terms that included the above, together with bacteria, antibiotics, food product, food safety, pathogens, auto inducer, food spoilage, biosensor markers, biological control, anti-cancer therapy, diagnostics and therapeutics, applications, as well as uses as part of their title, or within their keywords and abstracts were selected. References were collated from these selected databases, such as Google Scholar, Interscience Online Library, PubMed, ScienceDirect, as well as Thomson Reuters Web of Science. We established both inclusion and exclusion criteria to enable us access properly the articles etc., and those we deemed relevant to our study, were utilized. We were mindful of the year of publication so that we captured the more recent articles where possible. Importantly, those studies that we believed not addressing the research question of our current terse review, both in content and context, were excluded. Besides, the authors in the process of conducting the literature synthesis, applied their discretion to extract information strictly focused on the objective of the study. Essentially, all the information considered relevant was used to elaborate the discourse of this review.

DISCUSSION OF FINDINGS

Understanding Bacteria Quorum-Sensing Mechanism/Process: Some Key Basics

The step-wise mechanism/process by which bacteria bring about quorum sensing is shown in Figure 1. Quorum sensing was first elucidated in a bioluminescent gram-negative bacterium called *Vibrio fischeri*, which is symbiotically associated with other marine animals.[13] The association was such that *Vibrio fischeri* produced light which could be largely employed by the host to attract the prey, find mates and avoid predators.[14] By production and accumulation of acyl-homoserine lactone in its environment, the bacterium can trigger the expression of a certain specific set of genes[15] leading to the biosynthesis of an enzyme complex which enables the bacterium to produce light at high cell density (Figure 2).

All quorum sensing systems make use of small secreted communication molecules called auto inducers (AIs). Those that were mostly studied can be classified into any of the following classes of compounds: acylated homoserine lactones (AI-1)[15-17] that are commonly employed by Gram-negative bacteria, signals by means of peptides (Auto inducing peptides (AIP))[18-20] that is commonly used by Gram-positive bacteria and auto inducer 2 (AI-2) that is employed by the two types of bacteria.[21] A third class called auto inducer 3 (Al-3) which has eluded structural characterization has now been described in enterohemorrhagic *E. coli* by Kim *et al*.[22] Auto inducer 3 regulates virulence in this Gram-negative bacterium[10] which is a common causative agent of food infection. In general, these compounds are involved in several physiological processes within a bacterial cell that includes resistance to antibiotics, conjugation of plasmids, motility, and biofilm production. These help the cell to adapt to their environments and survive adverse conditions.[23]

The first step in quorum sensing is the bacterial cells producing tiny diffusible signal molecules, which then accumulate within the confined surroundings where there are situated. As the bacterial population continues to increase, it would reach a point where the signal molecules would exceed the threshold concentration. Through signal reception and transduction, the modulation of gene expression is triggered. To go into further details, quorum sensing, as is found in bacteria, is hinged on three fundamental principles: Firstly, bacterial species in the community must produce the AIs. At low population/cell density, the AIs diffuse into the environment and thus will be present at amounts not up to the critical levels needed for their detection. At higher population/cell density, the aggregate synthesis of the AIs will lead to a localised high aggregation of molecules which enables them to be detected for the cells to mount a response. Secondly, the AIs are recognized by receptors that are located in the cell's cytoplasm or the plasma lemma. Thirdly, there will be an expression of genes important for the cooperation of the cells and once AIs are detected there will be activation of their production.[24]

Note worthily, this cellular mechanism of signaling in bacteria involves the synthesis, liberation, and detection of molecules called auto inducers (AIs).[25] These AIs are commonly liberated in reaction to changes in the environmental conditions that include stress, limitation in nutrient availability, the osmotic shock that may induce the cell to produce mutagenic reactions to transcription and translation. These AIs increase in the environment of the bacteria as their population density elevates and these bacteria observe the information to track

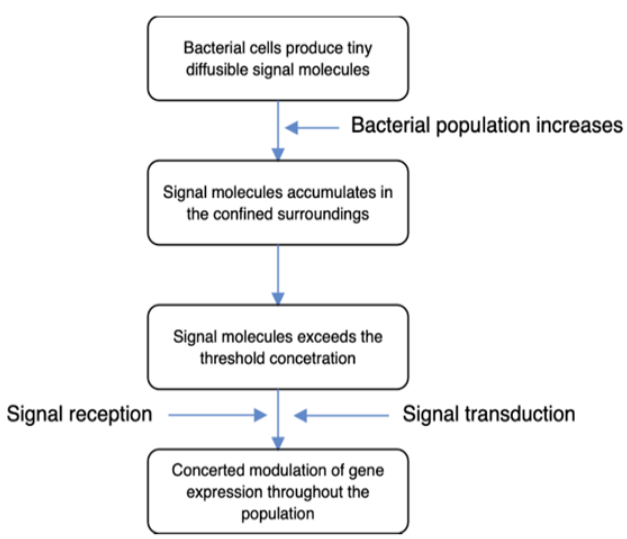

Figure 1: Basic step-wise mechanism/process by which bacteria bring about quorum sensing.

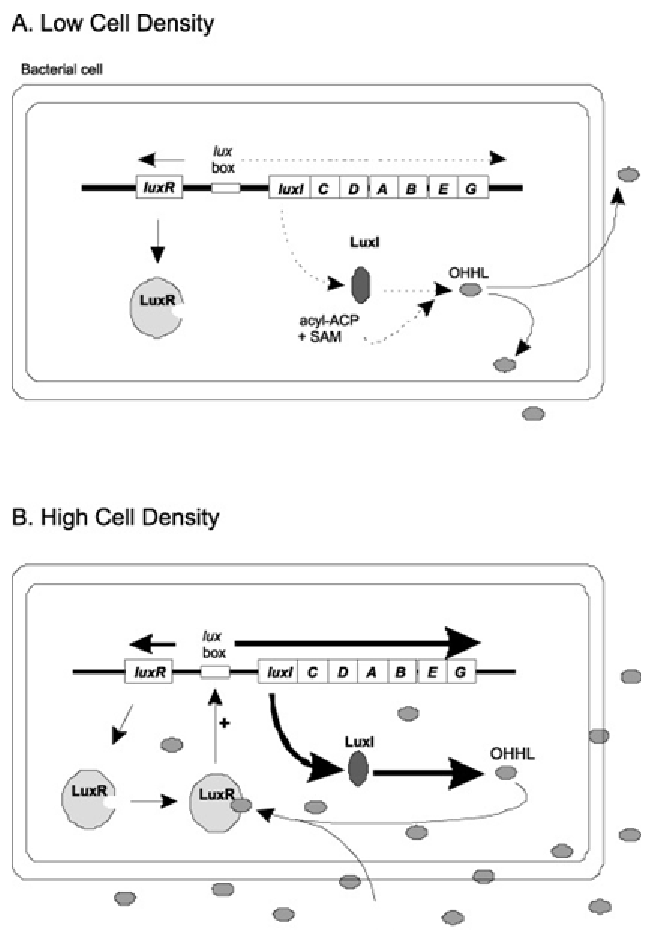

Figure 2: The regulation of bioluminescence in *V. fischeri*: the quorum-sensing paradigm, where (A) shows the low cell density, and (B) shows the high cell density. (Source: Whitehead *et al*.,[9] with permission from Oxford University Press)

the changes in their population and as a group alters the expression or appearance of certain genes in their cells.[26] Quorum sensing control genes oversee activities that are useful to cells when carried out by groups of bacteria that act in unison. Some of the activities of bacterial cells controlled by quorum sensing are the formation of biofilm, spore formation, production of antibiotics, competence, and secretion of virulence factors.[26] The function of cellular signaling/quorum sensing in the initiation of pathogenicity in bacteria is well established.[27,28] The discovery that quorum sensing signals play important roles in food spoilage has introduced a new aspect that researchers utilise to understand better the intricacies about food spoilage processes.[29,30]

DISRUPTION OF QUORUM SENSING IN BACTERIA

Several strategies can be employed to disrupt quorum sensing in bacteria. These include the following;

a. Quorum sensing receptor inactivation

Paczkowski *et al*.[31] in their study have shown that flavonoids that are known to possess antioxidant activities can bind to quorum sensing receptors thereby significantly reducing the expression of virulence genes in *Pseudomonas aeruginosa*. Studies have also shown that the structural analog of AHL signals, N-decanoyl-L-homoserine benzyl ester can reduce the synthesis of elastase and rhamnolipid which are virulence factors found in *Pseudomonas aeruginosa*, by obstructing the corresponding receptors in *Pseudomonas aeruginosa*.[32-34] It has also been found that metabromo- thiolactone can prevent *Pseudomonas aeruginosa* infection by decreasing the synthesis of pyocyanin thus preventing the production of biofilm.[35] AHL analogs capable of binding with LasR, LuxR, and TraR, receptors found in *Vibrio fischeri, Pseudomonas aeruginosa,* and *Agrobacterium tumefaciens,* respectively have been developed by Geske *et al*.[36]

Quorum sensing signals synthesis inhibition

Studies have shown that the synthesis of quorum sensing signals can be inhibited in bacteria. AHLs are molecules that take part in bacterial cell-to-cell communication. Inhibition of their synthesis can reduce AHL-mediated virulence factors in bacteria.[37] Priyadarshi *et al*.[38] and Surolia and Surolia[39] have shown that triclosan can reduce the synthesis of AHL by preventing the synthesis of precursors of enoyl-ACP reductase, but triclosan is considered a risk to human health.[40]

Degradation of quorum sensing signals

There can be disruption of communication among bacteria through degradation of quorum sensing signals by enzymes without causing any harm or damage to the bacterial cell. These enzymes include acylase, oxidoreductases, lactonase, and 3-Hydroxy-2-methyl-4(1H)-quinolone 2, 4-dioxygenase. Acyl Homoserine Lactone (AHL) lactonase has been revealed to stop infection by bacteria, elevate sensitivity to antibiotics, prevent the formation of biofilm and inhibit the extracellular proteolytic activity as well as pyocyanin synthesis in some bacteria such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.[41-44] The acylases brings about their action by breaking down amide bond in AHLs.[45-47] They have been shown to reduce the growth of *Pseudomonas aeruginosa*.[48,49] The dioxygenase on the other hand has been found to prevent quinolone signals in *Pseudomonas aeruginosa*.[50] The enzyme is capable of degrading signals mediated by 2-heptyl-3-hydroxy-4 (1H)-quinolone thereby decreasing the aggregation of signaling molecules within the bacterial milieu, thus reducing the discharge or release of pyocyanin, lectin, and rhamnolipid.[51,52]

b. Blocking of quorum sensing using antibodies

Studies by Kaufmann *et al*.[53] have shown that RS2-1G9 antibody is capable of binding to 3-oxo-C12-HSL in the environment outside of the *Pseudomonas aeruginosa* cell, thus causing the attenuation of the response to inflammation by the host. The antibody XYD-11G2 has also been revealed to mediate the breakdown of 3-oxo-C12-HSL signaling system, thereby preventing the synthesis of pyocyanin in Gram-negative bacteria.[54,55] Other studies have shown that the antibody AP4-24H11 can block the quorum sensing signaling system of *Staphylococcus aureus* and can remarkably reduce the tissue necrosis inside of the infected model.[56,57]

Use of a combination of antibiotics and anti-quorum sensing agents

This strategy is very effective in the treatment of certain bacterial infections.[58,59] A study using a combination of azithromycin, gentamicin, and curcumin revealed that they had a synergistic effect on the expression of virulence genes in *Pseudomonas aeruginosa*. Supplementation with curcumin led to a reduction in the doses of the antibiotics applied.[60] Several other studies conducted by various researchers involving the combination of various antibiotics (ciprofloxacin, tobramycin, gentamicin, colistin, tetracycline, lactam antibiotics) and anti-quorum sensing compounds such as caffeic acid, horseradish extract, and gallocatechin 3-gallate have demonstrated synergistic effects on the target bacteria used for the study.[61-64]

CONTROL OF QUORUM SENSING SIGNALS IN BACTERIA: SOME KEY APPLICATIONS/ USES

Food spoilage and quorum sensing signals

Various cellular signaling compounds that include auto inducer-1 and auto inducer-2 develop and increase in amount in varying food materials like meat, milk, and various vegetables.[30,65] Research studies have suggested that these signaling compounds are usually synthesized by certain micro-organisms that make up the initial microbial population in the food (specific spoilage organisms: SSOs). They commonly belong to the genera of the family *Aeromonas* spp, *Enterobacteriaceae, Pseudomonas* spp., and various lactic acid bacteria.[66] These groups of bacteria have been shown to usually cause the spoilage of meat and vegetable products; however, this depends on the type of food product and the conditions of storage they are exposed to.[67] In some foods, bacterial initiation of food spoilage may be regulated by phenotypes controlled by quorum sensing. Several enzymatic activities such as proteolytic, chitinolytic, lipolytic, and pectolytic activities, linked to the deterioration and spoilage of foods, are potentially regulated by quorum sensing.[30,68] Interrupting the quorum sensing circuit could be a useful way to control microbial gene expression linked to bacteria-causing food spoilage and infection in humans. Evidence from researchers has demonstrated that food spoilage due to bacteria could be controlled or regulated by QS signals.[20]

With the evidence that quorum sensing signaling systems are involved in food spoilage, it thus means that impeding and or control of cellular communication could be a potential way to stop and/or delay spoilage of food materials. Such a method which has been referred to as Quorum quenching (QQ) has been investigated extensively though their application in food preservation is scarce. Several compounds are known to block quorum sensing (Quorum sensing inhibitors) that do not affect the growth of bacteria. These include the natural furanones that are halogenated which are present in *Delisea pulchra,* a red alga, and several other derivatives that are synthesized that possess similar structures with AHLs, and inhibit expression of genes mediated by AHL through interference with auto inducer which binds to the lux R homologue.[69,70] The Quorum sensing inhibitors (QSI) are effective in the reduction of some virulence strains of *Pseudomonas aeruginosa* and *Pseudomonas carotovora*.[71]

Furthermore, several enzymes that breakdown AHL has been discovered in some bacteria, where they show QQ activities (Dong *et al*. 2000). For instance, the AHL lactone from *Bacillus* 240Bi hydrolyses the lactone bond in AHL leading to decreased extracellular pectolytic enzyme activities and attenuated pathogenicity on potato, eggplant, celery, cauliflower, and tobacco.[72] There have also been researches as well as results that demonstrated the function of quorum sensing inhibitors in slowing down the clotting process of milk, as well as the inhibitory properties of furanone C-30 in meat spoilage.[73] Some compounds, besides being extensively used in the food and flavour industries, are capable of obstructing the processes leading to quorum sensing in bacteria, thus, promising as food preservatives. Thus far, there appear not many investigations that have targeted their potentials as food preservative agents.[74]

Quorum sensing signals in antibiotic resistance

As a result of the widespread resistance to antibiotics by bacteria which today has turned out to be a major global challenge in the efforts made in combating various infectious diseases, therapeutic methods that aid in the avoidance of uncontrolled and casual use of antibiotics are usually given particular attention and consideration. Given the importance of quorum sensing phenomena in the control of pathogenicity of certain bacteria like *Pseudomonas aeruginosa*, an entirely new generation of antibiotics can be produced based on their inhibition of the quorum sensing system. These inhibitors can be applied synergistically with other medications to reduce the application doses of the antibiotics. It is thus possible to remove or reduce drug resistance in infectious bacteria through the inhibition of the quorum sensing regulatory process in such infectious bacteria.[75,76]

However, some of the halogenated furanones currently investigated were shown to be chemically reactive, unstable, and very toxic to be applied in the treatment of human bacterial infections[77] and may be lethal when applied on some animals like rainbow trout.[78] This has prompted screening for new quorum sensing inhibitor compounds and the development of quorum sensing inhibitor detectors or selectors.[79,80] Among these newly identified quorum sensing inhibitor compounds are extracts obtained from garlic as well as 4-nitropyridine-N-oxide which were found to be very effective in the reduction of biofilm tolerance to treatment with bramycin.[80] Other quorum sensing inhibitors are

Penicillium secondary metabolites; patulin and penicillic acid which reduced the virulence of *Pseudomonas aeruginosa*.[81]

Several studies have shown that a combination of anti-quorum sensing compounds and antibiotics can be very effective in the therapy of certain infections caused by bacteria.[58,59] Researches by various workers have demonstrated synergistic effects of such combinations on some target bacteria used for the study.[60-64]

Quorum sensing signals as biosensor markers

Results from some studies suggest that bacterial whole-cell quorum sensing biosensors can be employed as markers to detect the occurrence of some bacteria capable of causing disease in specimens from hospital and environmental sources. In general, these quorum sensing biosensors are made up of two major parts which are as follows: a construct from a plasmid that contains an AHL amenable regulator that controls the rate of expression of the target gene, relatory promoter-reporter gene, and a bacterial host cell. Thus, quorum sensing signals could help establish how pathogenic bacteria occur in polluted environments and groundwater, meat, and products produced from milk. An example is found with PSB406 and PSB1075 plasmids that serve as host cell quorum sensing biosensor systems for detecting some AIs of *Pseudomonas aeruginosa*. Each of the plasmids is made up of an R-protein producing gene and a reporter gene activated by a specific protein AHL complex.[82] It is also known that some lactic acid bacteria (*Lactobacillus* spp., *Leuconostoc* spp) that have Generally Recognised As Safe (GRAS) status could (safely) serve as a transporter host of reporter plasmids.[83]

Quorum sensing signals for anti-cancer therapy

3-oxo-C12-HSL that is found within *Pseudomonas aeruginosa* could serve as a quorum sensing signaling compound, which could prevent the spread and inducers of apoptosis in breast cancer cells from humans. Thus, it can be regarded as a candidate in the form of a drug, useful in the treatment process of cancers in humans. Quorum sensing signal can therefore be a good point to start in the development of synthetic AHL homologs that possess the ability to prevent cancer and also reduce side effects.[84] However, some researches conducted on mice have also revealed that various bacteria like *E. coli* and strains of *Listeria monocytogenes, Vibro cholera, and Salmonella typhimurium* can localize and proliferate in solid tumors, probably through surveillance of the host immune system that protects against attack by the immune system of the host.[83] Hence bacterial clusters can be employed in the production of biosensors that are capable of targeting cancerous cells. Thus it is probable that this can be realized by constructing artificial genetic circuits that can discern cancer microenvironment conductions or surface antigens on cancer cell surfaces.[85] Furthermore, it is possible to design whole-cell quorum sensing biosensors and gene delivery messenger systems that could have the capability of recognizing cancer cell aggregations *in vivo*.[86]

Quorum sensing signals in biological control

There is a technique called 'quorum quenching (QQ)', which has been considered as an alternative method of controlling bacterial pathogens via AHL-based QS mechanisms in regulating pathogenicity. The strategy employs several methods that will artificially increase the amounts of AHLs. Such methods include the addition of a gene that directly codes for AHL synthase into the cell of the plant, use of bacteria that degrade AHL to offer some level of protection to plants of interest, and heterologous expression of genes that encode for enzymes, enabling the degrading of AHL in either tissue of the plant or pathogenic organism. The bacteria in turn, misinterpret the actual size of the population, to produce virulence determinants much earlier compared to the population of pathogen big enough to support infection.[87] An example of this study is shown in transgenic potato and tobacco plants that expressed the AI lactone gene and manifested strong resistance against infection by *Pseudomonas carotovorum*.

Quorum sensing signals in diagnostics and therapeutics

The majority of the quorum sensing signals so far recognize gram-negative AHLs. There have been suggestions that QS signals could be employed as markers to enable the detection of the presence of bacteria that cause infections and disease in various specimens from hospitals and the environment. The enteric pathogen EHEC (*E. coli* 0.157:H7) has been projected to be accountable for over 70,000 disease conditions and 60 fatal cases in the United States alone.[88] It could therefore be possible to design genetic circuits for recognition of EHEC surface antigens like the somatic O antigen. The information obtained could thus be linked with QS such as a signal amplification module and eventually converted into an understandable output or modifying an already existing QS receptor to enable recognition of the surface antigens of pathogenic bacteria.[89]

For the future, designs may be directed towards the creation of whole-cell biosensors that can be ingested by the introduction of quorum sensing-based biosensors into micro-organisms with GRAS status (Generally Regarded As Safe) enabling detection of the presence of pathogens in the gut microbiota.[88] Various LABs and certain other bacterial genera have been previously reconstructed through genetic engineering to provide compounds with therapeutic use as well as vaccines to the intestinal mucosa.

SOME FUTURE PROSPECTS OF QUORUM SENSING SIGNALS

In the future quorum sensing could be applied in areas such as biofouling reduction, biofuel production, biodegradation as well as winemaking. Some briefs about these promising areas are below:

Biofouling reduction: The initial step in the establishment of biofouling is the production of a biofilm. Therefore having a good knowledge of the immediate and incidental consequences of quorum sensing signals and their inhibitors, and how to control them in the process of marine biofouling is of importance. In continuous bioreactor operations, studies have shown the abundant production of AHLs with N-octanoyl- homoserine[90] thus giving credence to the close relationship between quorum sensing and fouling of the membrane. The disruption of these auto inducers can be investigated to reduce membrane fouling.

Production of Biofuel: The current technologies employed for the conversion of lignocellulosic materials to biofuels appear negatively affected by the high cost of the various processing steps, such as initial treatments applied to the lignocellulosic material, breaking of the lignocellulosic material into component sugar units (saccharification) and recovery of products. Some processes mediated by quorum sensing may thus improve the potentials of producing biofuel from these lignocellulosic materials.[91] This can involve the use of some enzymes involved in hydrolysis at the biofilm substrate interface to enhance/elevate the rates of reactions and the possibility of the formation of a fungal-bacterial symbiotic association that will allow saccharification, hence enabling the optimization of the biofuel production process.

Biodegradation

There has been an increasing awareness of the harmful effects of environmental pollution. This has led to an increase in the search for more efficient and faster strategies that may be employed in the cleaning of polluted environments and sites. Quorum sensing-based bio organics have been suggested to aid in the environmental restoration of polluted sites. Yong and Zhong[92] in their study reported an enhanced and elevated degradation of phenol by *Pseudomonas aeruginosa* through the inclusion of AHLs exogenously. However, this perceived involvement of quorum sensing in biodegradation needs further studies.

Winemaking

Certain techniques hinged on the application of quorum sensing have been employed in winemaking. Wine production depends heavily on the various activities of yeast and bacteria for the production of certain desired flavours in the product. Striking a balance in the yeast-yeast interactions against the yeast-bacterial interactions could have a remarkable influence on the end product.[93] There have been suggestions that using quorum sensing in achieving and maintaining a balance in such a relationship could open new ways of ensuring that the desired quality attributes of a certain product are achieved.

CONCLUSION

This terse literature review has provided a snapshot of quorum sensing signaling in bacteria, specifically attempting to throw more light on the mechanism, its discovery, and involved molecules, to its applications/uses. Specifically, we have shown the basic step-by-step mechanism by which bacteria bring about quorum sensing. Understanding bacteria quorum sensing mechanism/process can be very challenging. Besides, the several strategies employed to disrupt quorum sensing in bacteria have largely involved receptor inactivation, signaled synthesis inhibition including its degradation, blocking of quorum sensing using antibodies, as well as a combination of antibiotics and anti-quorum sensing agents. There is hope in the future for application of quorum sensing technique, as it could be applied in areas such as biofouling reduction, biofuel production, biodegradation as well as winemaking, thus it is possible that through this, prospects for the development of future novel processes can be achieved.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

AIs: Auto inducers; **AI-1:** Auto inducer 1; **AI-2:** Auto inducer 2; **AI-3:** Auto inducer 3; **AIP:** Auto Inducing Peptides; **AHL:** Acyl Homoserine Lactone; **EHEC:** Enterohemorrhagic *Escherichia coli*; **GRAS:** Generally Regarded As Safe; **SSOs:** Specific Spoilage Organisms; **QS:** Quorum Sensing; **QSI:** Quorum Sensing Inhibitors; **QQ:** Quorum Quenching.

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