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Research Article

Quorum Sensing in Bacterial Pathogenesis

Abstract

Introduction: Quorum sensing (QS) in meaning word is a system of stimulus and response correlated to a fixed number of microbial Population density which make the microbes sense and awareness of the presence of bacteria and their community. Bacteria in social life, the greatest benefit from the competitive environment to get the genetic regulatory mechanisms they use.

Materials and Methods: This paper is a review article through library research and internet search sites, PubMed, Sid, Google Scholar keyword (Quorum sensing, AHL, pathogenesis) is collected in the years 2005 to 2014.

Results: Quorum sensing in bacteria (pathogens and non-pathogens) regulates cell activity in quickly adapting to changing environmental conditions for maintenance and survival of bacteria in the environment. Process that is regulated by Quorum sensing including biofilm formation, Conjugation, produce virulence factors, toxin production and escape from the immune system. In this paper, we investigate the existence QS in gram-negative and gram-positive bacteria and its role in the pathogenesis of some of the major virulence factors are discussed.

Conclusions: Increased prevalence of bacterial strains resistant to antimicrobial drugs is a big problem to find a new way to treat these infections is important. QS System to prevent damage to the opportunity to respond to the signal and prevent the bacteria express virulence factors follows. My hope is that by using antagonists and agonists can control so many dangerous diseases.

Introduction

Bacteria in the collective and social life for the greatest benefit of the competitive environment in case of genetic regulatory mechanisms of communication called Quorum sensing (QS) is used. Quorum literally means an assembly or a fixed number of each class of objects called QS means of microbes and their community is aware of the presence of bacteria. Quorum sensing in all bacteria (pathogenic and non-pathogenic) regulate cell activities in quickly adapting to changing environmental conditions and to maintain the survival of bacteria in the environment. Process that is regulated by Quorum sensing including biofilm formation, Conjugation, Sporulation, produce virulence factors, invasion and toxin production is [1-3].

In this paper, we investigate the QS in the gram positive and gram negative of bacteria and its role in the pathogenesis of some of the major virulence factors have been examined in the following factors in prokaryotes and eukaryotes suggests that these molecules parser. It is hoped that the use of antagonists and agonists can be used to control most dangerous infectious agents.

Quorum sensing History

In 1970, for the first time the QS was observed in *Vibrio fischeri* bacterium. The researchers found that the Gram-negative bacterium that lives in a free-living in the seas and oceans. The low number does not produce luciferase but when the luminous organs of fish or marine bacteria holes cephalopods (*Euprymna scolopes*) into the holes where the organs of reproduction is and then increase the number of bacteria, QS active and causes the activation of luciferase gene and luminance phenomenon occurs.

Signaling mechanisms in prokaryotes

Prokaryotes for messaging cell to the different mechanisms of pheromone-like peptide-modified peptides, QS and intracellular kinases are activated. Table 1 shows the mechanisms of bacterial signaling and its role in the processes shown in [5].

As can be seen in its response induced peptide pheromone QS and a large number of bacteria involved.

Micococcus geztantuse, a Gram-negative bacterium found in soil, if bacteria grow again in appropriate circumstances is removed layers and bacteria will multiply. The stages of differentiation by extracellular signals to produce small peptides are the KD17 forms. *Bacillus subtilis*, two different peptide which is capable of being used for transformation and spore formation it is necessary [2,3].

QS in Gram-negative bacteria

As noted above QS concept first discussed in gram-negative bacteria Pathogenic and non-pathogenic. Gram-negative bacteria

Table 1: Community bacteria together with different mechanisms of cell-to-cell signaling.

Messenger molecule	Process or mechanism of bacteria
Peptide pheromone	Sporulation and the formation of a hard object in <i>Micococcus geztantuse</i>
Peptide pheromone	Conjugation in <i>Enterococcus fecalis</i>
Modified peptides	Differentiated morphology in <i>Streptomyces Cuiceilar</i>
Hemoserin acyl lactones (AHLs), peptide pheromone	Self-induction of the number of bacteria

or molecules that self-discharge phenomena such as biofilm formation, virulence, move, produce antibiotics, luminance and plasmid transfer can be involved. QS in the pathogenesis of bacteria such as *Pseudomonas aeruginosa*, *Burkholderia Cepacia*, *Salmonella typhimurium*, *Yersinia enterocolitica*, *Escherichia coli*, *Vibrio cholera* and *Serratia species* [2,3].

QS in Gram-positive bacteria

In Gram-positive bacteria such as gram-negative bacteria, QS has role triggering of infection, antibiotic production, biofilm, and so is the role and structure of QS molecules in Gram-positive bacteria differ from gram-negative bacteria (Figure 1).

In the gram positive bacteria the QS have more molecules of peptide Octa or Hepta who called pheromone involved in transmitting messages. These molecules that are hydrophobic low molecular weight ($5 \times 10^{-11}m$) and at least two molecules per cell of these peptides with biological activity there. Receptor agonist study suggests that these molecules messaging system are similar to cytokine signaling in eukaryotic cells. QS in various gram-positive bacteria such as *Staphylococcus aureus*, *Bacillus* and *Actioiomycetes* been observed and studied [2,3].

Types of QS molecules

Unless, of bacteria with similar auto inductor communicate with each other, and because any bacteria to induce the same way it responds to various types of inductor in bacteria is discussed. The most important signal to the cell-cell communication in bacteria was discovered for the first time as Acyl- Homoserine Lactone (AHL), which is only produced in gram-negative bacteria and a lactone ring and side chain in its structure (Figure 1). Different bacteria produce different AHL molecules that differ in the side chain. It should be noted that the side chain of the lactone ring QS activity is essential for any changes (create unsaturated bonds or the formation of large groups), auto inductor activity is affected. For example, if the lactone rings of *Vibrio fisher* Homoserin be used instead of homocysteine-induced decreases its activity [2,6-8].

Gram-negative bacteria as signal molecules in the cell-to-cell communication used are: AHL, Thiolactone ring (AIP), hydroxyl palmitic acid methyl ester (PAME), Foranozil methyl borate (AI-2) and Dodicanoic acid methyl (DSF) [2,3].

It should be noted that QS is not only restricted to prokaryotes and eukaryotes, particularly fungi are produced and these molecules are

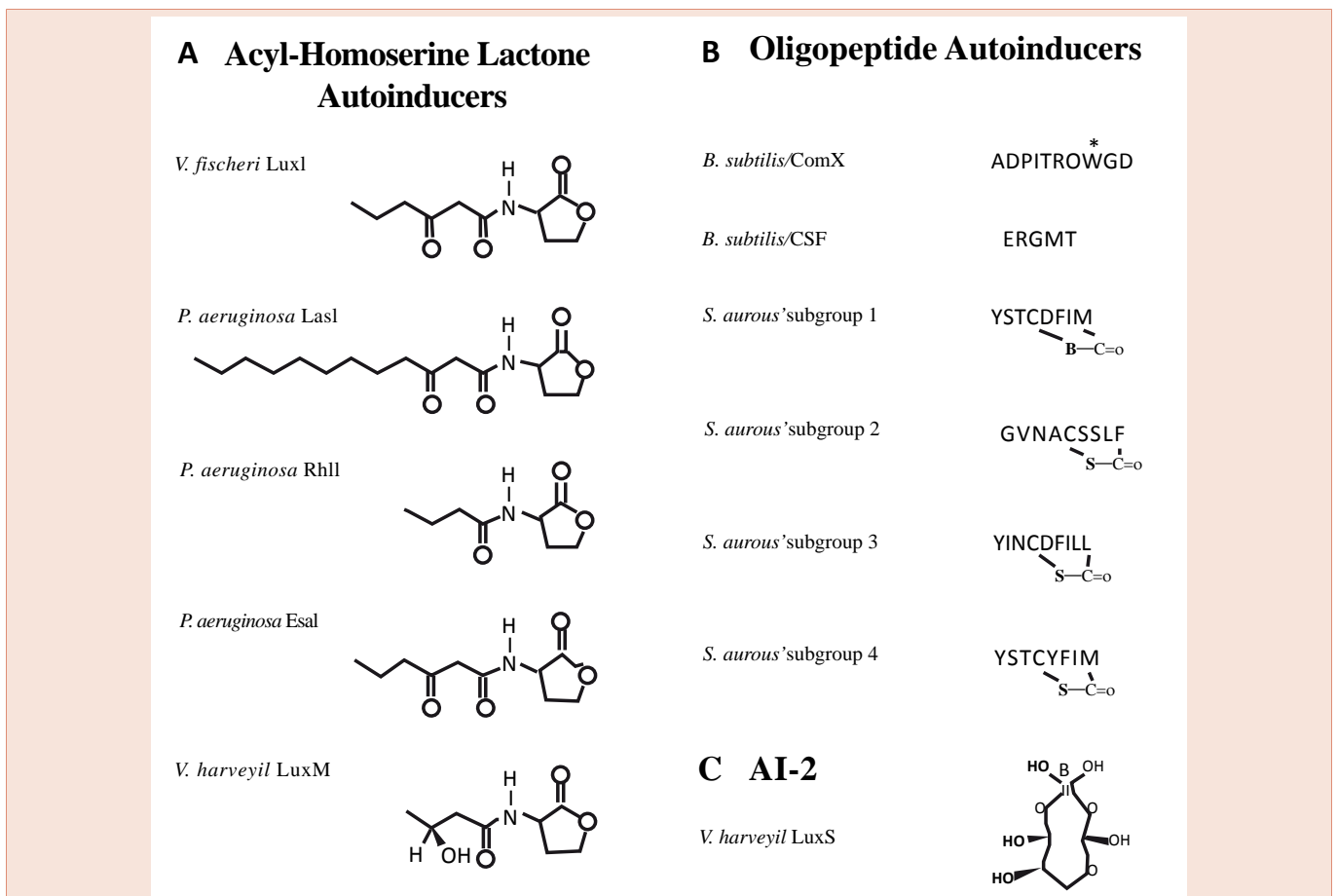


Figure 1: Different types of buildings are auto inductor (AI) in positive and Gram-negative bacteria.

involved in their pathogenesis. For example, *Candida albicans* with Foranozoeik acid (FA), has become a form of yeast to the mycelium form has an important role in the pathogenesis of controls [2].

Molecular mechanisms messaging QS

QS to convey a message to the protein ProI (auto inductor) and ProR (transcription factor receptor) (Figure 2). As can be seen messaging system is controlled by the genes involved in virulence genes *i* and *r* is controlled by a protein complex RI. The complex, RI, ProR and ProI genes encoding transcription regulatory feedback mechanism to enable or disable when the system was too much ProI in connection ProR transcription factor is the increase in the production of AI [9-13].

QS in *Vibrio fisher*

Cephalopods are illuminated when the bacteria enter the tissues where it accumulates at a concentration of 10^{11} ml AHL produces the molecule activates luciferase gene produces light at night. The bacterial Lux I Homologous ProI and LuxR Homologous is ProR. When these two proteins were formed together in addition to the control of RI, LuxI and LuxR of the genes involved in the production of light (Figure 2), [4,10,11].

QS in *Vibrio cholera*

Vibrio cholerae causes cholera is to produce exotoxins. It consists of 20 genes involved in the pathogenicity of the bacteria has a Regolon the production and secretion of toxins and genes required for survival in host cells. These genes regulate transcription Regolon *toxT*, *tcpP* / *I*, *toxR* a cascade controlled. The adjustment to external factors such as temperature, pH, osmotic pressure, and so respond. It is now clear that QS is involved in the regulation of these genes (Figure 3) [14].

QS in *Pseudomonas aeruginosa*

Pseudomonas aeruginosa a gram-negative bacilli that due to the high resistance of biofilms to antibiotics, variation in the nature and cause severe nosocomial infections in the hospital. Studies show that the bacterium is an opportunistic pathogen of more than 600 genes is controlled by QS. The QS and biofilm formation in a high drug

resistance in bacteria is essential. If using QS and its antagonists, biofilm inhibition may be a chronic infection and drug resistance in the bacteria solution of the above.

Pseudomonas aeruginosa QS system has two named RhlR / I and LasR / I is.

System LasR / I, Regolon *rhl* pathogenicity genes *toxA*, *apr*, *lasA*, *lasB* controls and systems RhlR / I, production of elastase (IL-2 has a breaking strength) controls. The bacteria with the help of the system, the ability to survive and multiply within cells are found (Figure 4), [16-18].

QS in *Staphylococcus aureus*

Staphylococcus aureus QS is related to several extra cellular protein toxins. These proteins are produced in different stages of growth and may be controlled by QS early stage of infection has spread to nearby tissues show. General accessory gene regulator *agr* operon has two important and one of the operon, a RNA molecule that encodes a unique name RNAPIII increased secretory protein expression and decreased expression of surface proteins. In contrast to the RNAPIII, a promoter region of a gene responsible for the expression of RNAPIII gene called four *agr* BDCA that these genes are essential for the expression of RNAPIII optimized. *AgrD* and *agrB* genes encoded a small peptide (QS). The production of these molecules was dependent on cell density and RNAPII and RNAPIII helps control gene expression (Figure 5), [20-22].

Analysis of molecules QS

Studies show that prokaryotes and eukaryotes great (especially mammals) with the production of enzymes, the QS molecules are decomposed, so we can help these enzymes, inhibit the microbial pathogenicity. In bacteria such as *Bacillus* spp and *Klebsiella pneumonia*, *Pseudomonas aeruginosa* AHL-degrading enzymes produced [27-29]. One of the enzymes in bacteria has been studied AHL - Quorum-Quenching Laktonaz that the enzyme activity and *aiiA* or *attM* coded by genes. *AiiA* gene in *Bacillus cereus* strains *uw85* code and makes the QS in bacteria inhibited *Chromobacterium violaceum*. Enzymes produced by different genes in *Bacillus* together

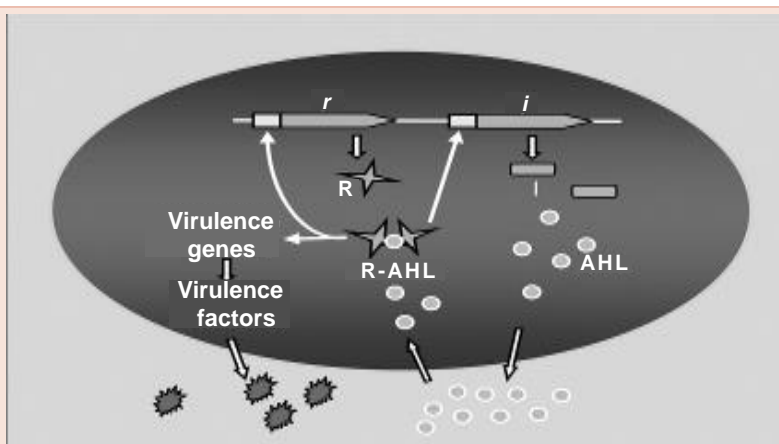


Figure 2: Molecules involved in signaling by QS.

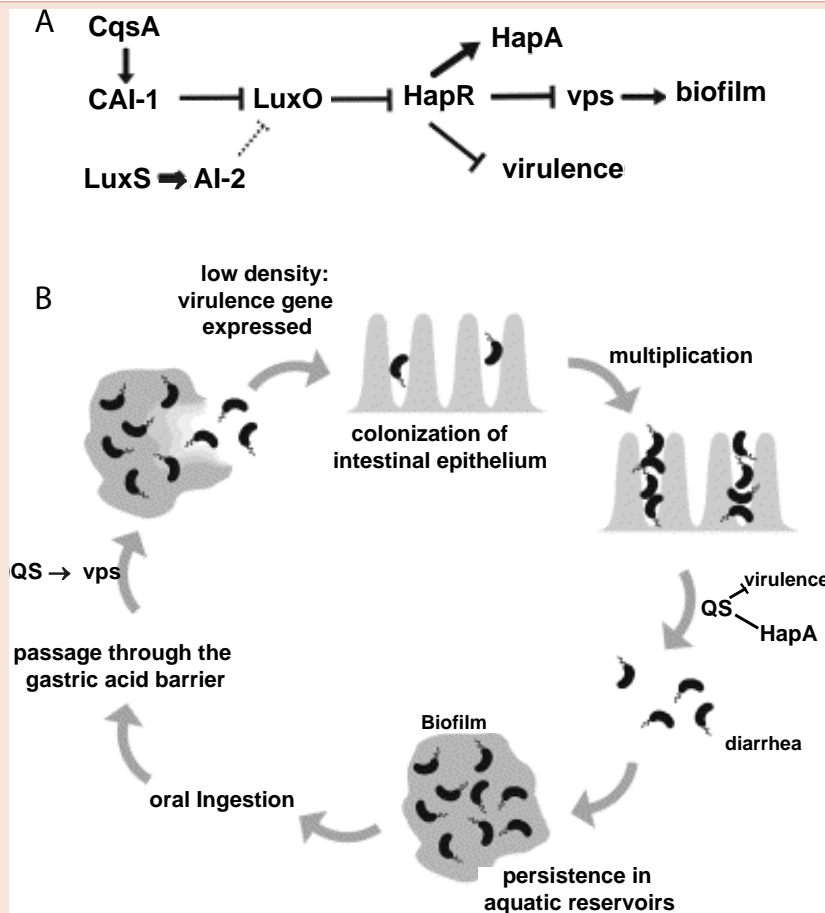


Figure 3: The role of QS in the *Vibrio cholera* in the intestine.

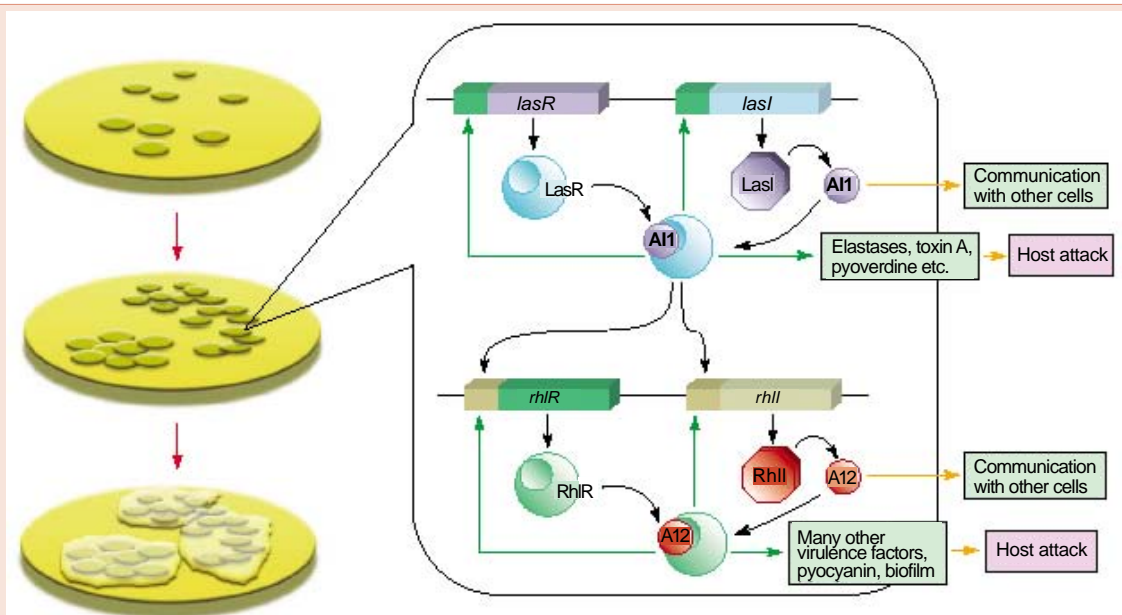
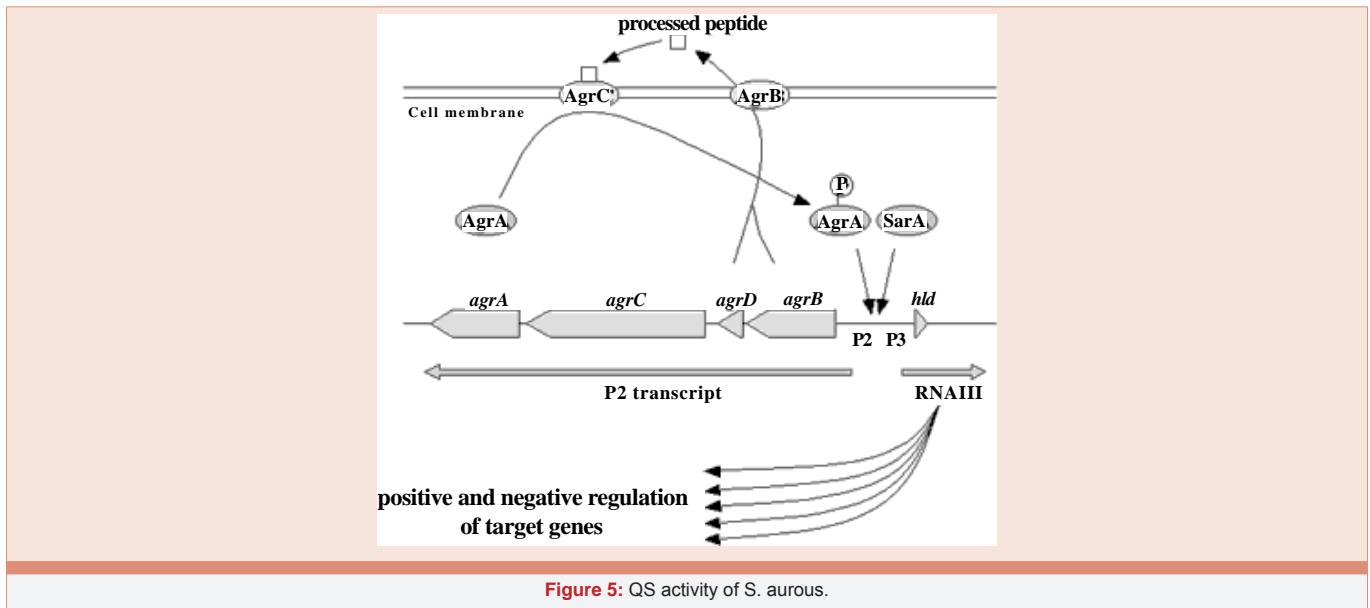


Figure 4: Activity of *Pseudomonas aeruginosa* QS.



have 90% similarity [30,31]. The human enzyme produced by epithelial cells of the airways Kh3- o-C12-HSL, C6-HSL (but not C4-HSL) breaks that some researchers believe that this is due to the production of enzymes Para-oxygenase (by only PoN3) and PoN1, break the lactone ring [31].

QS Antagonists

The control of pathogenic bacteria, consider different ways. One of them, the microbes is QS control. To this end, researchers from a variety of natural and synthetic antagonists have been used to control QS. Auto inducator a natural antagonist, Foranoz is produced by a type of algae called *Delisea pulchra* and is used to prevent the bacteria.

This natural compound sterile barrier SwrR-C- reactive and preventive action LuxR-3-Oxo-C6- HSL and CarR-3-oxo-C6- HSL in *Vibrio fisher* but on LasR-oxo- C12- HSL *Pseudomonas aeruginosa* is less effective. Some synthetic antagonists due to changes in the (3-Oxo- C12-D10) Foranoz ring chain length fatty acids and prevents biofilm formation in *Pseudomonas aeruginosa* is able to reduce the number of pathogens.

The antagonists are likely “to avoid being LasR dimer that is essential to avoid duplication and transcription activation are pathogens [31,32].

Conclusion

Increased prevalence of bacterial strains sustained antimicrobial drug and multi-drug resistant strains is a huge problem to find a new way to treat life-threatening bacterial infections require. The QS system is an opportunity to prevent the destruction of bacteria to respond to signals and inhibit the expression of virulence factors cause. The AI is designed drugs inhibiting the biosynthesis process. The therapeutic approach in addition to inhibiting the production of virulence factors, the intervention of differentiated biofilms, and bacterial sensitivity to antibiotics has increased [33]. QS, a method by which bacteria communicate with each other and in this way you can tune

into their genomic expression patterns in the face of environmental change. QS In all Gram-negative bacteria is dependent on cell density and bacteria, Gram-positive bacteria and AHL molecules such as small peptides are called pheromones. These molecules are caused by bacteria that grow out or not growth, toxin producing or not producing. *Staphylococcus aureus* in the stationary phase and *Vibrio cholera* toxin is produced in the logarithmic phase. *Mycobacterium tuberculosis* in the logarithmic growth phase, which are invasive procedures regulated by QS. Research shows that prokaryotes and large eukaryotes (especially mammals) with the production of enzymes, the QS molecules are decomposed, so today antagonists and agonists of reducing pathogenicity of infectious agents such as *Pseudomonas aeruginosa*, *Vibrio cholera* and *staphylococcus aureus* [11,28]. Also today with restrictive QS, anti-bacterial drugs produced in the control of infections in medical, agricultural and industrial applications [28,29].

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