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Review Article
Quorum Sensing Inhibitors/antagonists Countering Food Spoilage Bacteria-need Molecular and Pharmaceutical Intervention for Protecting Current Issues of Food Safety

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Abstract
Microbial activity is considered as an important cause for the manifestation of food spoilage. The detection of chemical signals sharing information between food spoilage bacteria present in food products has initiated a new dimension to formulate an alternate preventive strategy against these spoilage bacteria. Quorum sensing or cell-to-cell communication is employed by a diverse group of bacteria talking to each other through the signaling autoinducer molecules. Based on potential of these molecules, Quorum-Sensing Inhibitors (QSI) or Quorum Quenching (QQ) compounds can be used as novel biopreservatives which abrupt the virulence of food spoilage microbes to uphold the nutritional quality of packaged and Ready To Eat (RTE) food and food by products. Through the pharmaceutical interventions and molecular mechanisms of intracellular, intercellular and interspecies communication via signaling molecules, preventive strategies can be formulated for production of pathogen free food products. Though identification of species specific signaling pathways is a challenging task for the food microbiologists and pharamacists but proper implementation of QSI molecules would be helpful for the food manufacturers in food processing plants through critical follow ups of Hazard Analysis and Critical Control Point (HACCP) to maintain the food quality and sound public health. This review draws the attention of researchers involved in dairy microbiology, meat and fish processing industries, packaging channels and neutraceuticals and pharmaceutical industries to explore the library of QS and QSI molecules to put forward and apply them as bio-preservatives for production of safe food products to meet the global food demands of growing world population.

Key words: Quorum sensing, spoilage bacteria, antibacterial activity, Ready To Eat (RTE) food, food safety, food industry, public health

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INTRODUCTION

Microbial pathogens infecting humans, animals, birds, fishes and spoiling foods are of major concern in the food industry as these cause tremendous economic losses and pose serious public health consequences (Dhama *et al*., 2013a). Increasing population expansion, changing life style and challenges of emerging infectious diseases including of food borne-pathogens warrants appropriate strategies to be followed for safeguarding nutritional security and food safety issues especially in the current era of one world-one health (Dhama *et al*., 2013b; Tiwari *et al*., 2014a). Food spoilage occurs due to natural aging changes and microbial activity which impart change in the texture of food evident as altered taste and off-odor. Attack of microorganisms while food preparation, processing, packaging or at supply/delivery counters lessen the shelf life of food products and cause significant problems in the food industry such as *Yersinia intermedia* and *Pseudomonas putida* bacteria are responsible for production of fruity off flavour in pasteurized milk (Whitfield *et al*., 2000; Yarwood and Schlievert, 2003; Bai and Rai, 2011). Food-borne pathogens of importance include *Salmonella* spp., *Eschericihia coli*, *Campylobacter* spp., *Listeria monocytogenes* and others (Dhama *et al*., 2013a, 2015a). Even with the application of food preservatives, excessive amounts of foods are lost due to microbial spoilage. The rapid emergence of drug resistant superbugs capable of resisting most commonly used antibiotics has emphasized the need for the development of novel strategies against microbial pathogens (Dhama *et al*., 2013c; Tiwari and Dhama, 2014). Conventional antibiotics kill or inhibit bacterial growth by interfering with essential housekeeping functions hence inevitably impose survival pressure to adapt new ways by microbial pathogens for prolonged survival and this phenomenon prompt scientists and researchers to look for alternative and newer therapeutic regimens viz., phages, avian egg yolk antibodies, cytokines, antimicrobial peptides, medicinal herbs/plant extracts, panchgavya elements, immunomodulatory agents and others (Dhama *et al*., 2008, 2014a, b, c, 2015b, c; Tiwari *et al*., 2014b; Zorriehzahra *et al*., 2016). One such promising strategy is the Quorum Sensing (QS) inhibition or quorum-quenching approach, also known as anti-pathogenic or signal transfer interference approach which disturbs the extracellular bacterial talk by interfering with microbial cell-to-cell communication also known as quorum sensing (Waters and Bassler, 2005; Dong *et al*., 2007; Williams *et al*., 2007). Fuqua and Winans (1994) pertinently termed this cell-to-cell communication as quorum sensing (Williams, 2007).

Quorum Sensing (QS) or cell-to-cell communication is employed by a diverse group of bacteria such as Brucella, Pseudomonas, Yersinia, Bacillus, Staphylococcus, Streptomyces and food borne pathogens as *Campylobacter* spp., *Listeria monocytogenes* which talk to each other by producing the signaling molecules and autoinducers. By the knowledge of quorum sensing among different species of bacterial pathogen especially in food borne pathogens their characteristic virulence mechanisms and pathogenesis can be regulated and blocked by employing natural or synthetic quorum sensing inhibitors or their analogues such as rutin, eugenol, ellagic acid, aspirin and malvidin to upset the pathogenesis (Novak, 2006; Parker and Sperandio, 2009; Vikram *et al*., 2010; Sarabhai *et al*., 2013; Zhou *et al*., 2013; El-Mowafy *et al*., 2014; Gopu *et al*., 2015). However, it is not easy to subside the communicating signals among food borne bacteria due to complex nature of food where they exist and proliferate at the expense of food quality (Bai and Rai, 2011). Quorum sensing as intercellular, intracellular and/or interspecies communication among (Gram positive and Gram negative both type) bacteria convene major role in bacterial pathogenesis to affect the end users and in spoilage of food, hence blocking these signaling channels can reduce the pathogenesis and hamper the food borne pathogen population (Whitehead *et al*., 2001; Smith *et al*., 2004).

Quorum-Sensing Inhibitors (QSI) or Quorum Quenching (QQ) compounds can be used as novel biopreservatives which abrupt the virulence of food spoilage microbes to uphold the organo-leptic, physical as well as nutritional quality of fresh, processed, packaged and Ready To Eat (RTE) dairy, meat and fish food and food by products for safer and sound consumer health (Nychas *et al*., 2007). Present review discussed diverse signaling molecules produced by different food spoilage and other pathogenic bacteria, molecules involved in signaling mechanism, role of signaling chemical transmitters in biofilm formation in the medical field and food industry, besides throwing light on potential candidates which can be used as quorum-sensing inhibitors for safe food production.

QUORUM SENSING (QS)

Quorum sensing elaborates that bacteria can communicate with each other and they are not only small, tiny, single or many in number, simple organisms inhabiting our world. Bacteria use signaling molecules to convey message to other bacteria by releasing signals into the environment. Through QS bacteria are also capable of measuring the number (concentration) of the molecules secreted within a population. The QS is the phenomenon in which the accumulation of chemical transmitters in the surrounding help closely present bacterial cells to assess the number of bacteria (cell density) present in the close vicinity. In the natural environment, different bacteria use various classes of signaling molecules and the outcome of bacterial interaction can be observed through various assays, biosensors and detection systems including multiple coupled reporter assays based on detecting bioluminescence, *lux*CDABE-based plasmid sensors for exploring N-acyl homoserine lactone-mediated quorum sensing, by observing cloned fluorescent green protein by observing expressed promoter colorimetric enzyme assay gene fusions, mutational complementations and with the wide elaborative knowledge of these signaling pathways quorum sensing among bacterial pathogens can be selectively inhibited (Winson *et al*., 1998; Annous *et al*., 2009).

The QS enables bacteria to co-ordinate with the rapidly changing environmental conditions in order to survive. These responses take account of adaptation with the available nutrients, defense against other microorganisms which may compete for the same nutrients and protect microorganisms from the changing environmental conditions. Pathogenic bacteria co-ordinate and changes their virulence in order to escape the immune response of the host for establishing successful infection (Turovskiy *et al*., 2007).

Presently, several QS systems exist among the various organisms such as marine bacteria and several pathogenic bacteria. There are several different classes of signaling molecule and different bacterial species use different molecules to communicate. At times single bacterial species may have more than one QS system and consequently use more than one signal molecule. They induce expression of different genes for production of desired protein molecule which corresponds to different outcome as per the signal.

The signalling molecules produced and secreted during bacterial growth include autoinducers and N-Acyl Homoserine Lactones (AHLs) which command the QS by modulating the gene expression in bacteria in concentration dependent mode (Nealson *et al*., 1970; Podbielski and Kreikemeyer, 2004). The concentration of these signal molecules increase with the growing population in the environment and when it attains a threshold level desired beneficial phenotypic effects are obtained through regulation and control of quorum sensing dependent target gene expression. As no external stimuli is involved in bacterial cell talk hence phenomenon is referred as autoinduction (Czajkowski and Jafra, 2009).

Two groups of signal molecules are involved in bacterial quorum sensing. One is the peptide derivatives typically used by Gram-positive bacteria, while Gram-negative bacteria exploit the fatty acid derivatives. The N-Acyl Homoserine Lactones (AHL) and autoinducer (AI-2) based quorum-sensing systems associated with Gram-negative bacteria in different food ecosystems have been detected (Fuqua *et al*., 2001; Taga *et al*., 2001; Van Houdt *et al*., 2004; Dong *et al*., 2007). The QS is omnipresent in many known bacterial species including Agrobacterium, Brucella, Bukholderia, Erwinia, Enterobacter, Pseudomonas, Ralstonia, Serratia, Vibrio, Yersinia, Bacillus, Enterococcus, Staphylococcus, Streptococcus and Streptomyces (Novick, 2003; Yarwood and Schlievert, 2003; Bottomley *et al*., 2007; Brackman *et al*., 2008).

Through QS cross talk, bacteria from one species can communicate with bacteria of another species also. This intercellular, intracellular and interspecies communication via QS is referred as quorum sensing cross talk which has implications in many areas of biology in general and microbiology particularly as in the biosphere homogenous or mixed species heterogenous populations can exist such as biofilms (Van Houdt *et al*., 2004).

Modes of actions of quorum sensing: Majority of bacteria follow two types of mechanisms for quorum sensing. They either employ Acyl Homoserine Lactone (AHL) mediated or autoinducing peptide (AIP) mediated approaches for the detection of QS signals, in response to which expression of target gene is modulated accordingly. Most of Gram negative bacteria perceived the signals through AHL molecules and Gram positive bacteria via AIP peptides. In Acyl Homoserine Lactone (AHL) mediated quorum-sensing systems signals are detected through a cytosolic transcription factor while in autoinducing peptide (AIP) mediated system signals are sensed through a membrane-associated 2-component response regulatory system. *Vibrio harveyi* is capable of communicating and responding through both the signaling mechanisms (Dong *et al*., 2005).

In AHL quorum sensing system mechanism depends upon bacterial density and as the population increases more signals are generated, they are accumulated initially and then released in the environment to be received by nearby cells. After signal reception by appropriate *lux*R receptor present in other bacteria autoinduction occurs in terms of target gene expression to generate the desired function via quorum sensing regulation. The AHL molecules are synthesized by *lux*I encoded AHL synthase (I-protein) by using S-adenosylmethionine (SAM) and acyl chains derivative of common fatty acid. The short-chain AHL signal can diffuse passively across the bacterial membranes but the long-chain AHL signals require active transportation for their exit and secretion. Secreted AHL signals combine with the R protins of

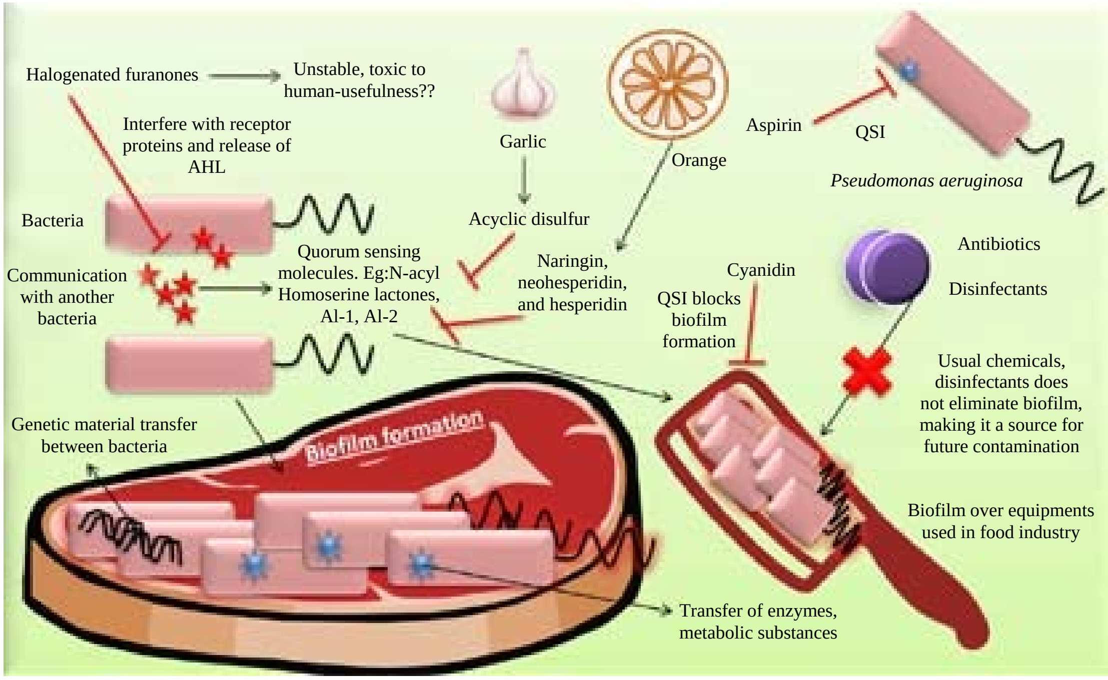

Fig. 1: An overview of the modes of action and applications of quorum sensing

lux R family to produce R-AHL complex which command the autoinduction and control the quorum-sensing regulatory functions. By using QSI compounds or AHL-degradation enzymes AHL signals can be interrupted, decayed or switched off to down regulate the quorum sensing dependent genetic expression and expected outcome (Huang *et al*., 2003; Schuster *et al*., 2004; Zhang and Dong, 2004). For autoinducing polypeptide (AIP) system ABC transporters are required, signals are detected by using 2-component sensor for amending the expression of quorum-sensing regulated gene through regulatory RNAs and intracellular transcription factors. Gram-positive bacteria mainly use autoinducing polypeptide (AIP) mediated signaling system which are mostly involved in intraspecies communication while Gram negative bacteria prefer autoinducer-1 (AI-1) and autoinducer-3 (AI-3) in QS system. The AI-2 is utilized for interspecies communication and can be used by both Gram-positive and Gram-negative bacteria (Schauder *et al*., 2001; Smith *et al*., 2004). An overview of the modes of action and applications of quorum sensing is depicted in Fig. 1.

QUORUM SENSING AND BIOFILM FORMATION

Group of bacteria that come together to form a slimy mass over any surface is called as biofilm. Biofilm formation is a cause of concern among various field of biology and is certainly a major problem among medical field where biofilms formed on prosthetic materials that are intended for surgery leads to infection thereby resulting in serious life threatening problems (Skandamis and Nychas, 2012). Biofilm formation has various advantages to the bacteria as they become resistant to disinfectants, antimicrobials, adverse environmental conditions, they also exchange metabolic substances and also genetic materials among the group members so that it becomes difficult to eradicate these organisms. Under these circumstances bacteria utilizes certain chemicals to talk among each other which is represented as QS. It is not the only medical field which suffer from the problem caused by biofilm formation, food processing industry also face similar problem where biofilms formed over the utensils act as a constant source of pathogen that contaminate the food products (Brooks and Flint, 2008; Bai and Vittal, 2014). Foodborne pathogens like *Listeria monocytogenes, Campylobacter jejuni, E. coli* O157:H7 and *Yersinia enterocolitica* are well known for its biofilm forming ability on food surfaces and also on the equipment, thus threatening the field of food processing industry leading to great economic losses (Bai and Rai, 2011). A novel quorum-sensing regulator molecule MqsR, B3022 is responsible for biofilm formation in *E. coli* through autoinducer 2 (Barrios *et al*., 2006). Biofilm formation has different stages and QS has been noticed in all stages. The same bacteria in the biofilm have a different genome program when compared to its free living counterpart (Asad and Opal, 2008). The QS plays a major role in regulation of metabolic activities thereby controlling the nutritional demand in the biofilm. Several studies report that QS has the leading role in biofilm formation. One of the contaminant organism of food industry (fish, meat and dairy products) *Hafnia alvei* is capable of existing as biofilm in the nature but results of experiment performed with *H. alvei* 071 *hal*I mutant showed that this pathogen lost its biofilm forming ability due to the loss of *hal*I showing that QS molecules are essential for formation of biofilm (Tan *et al*., 2014). Formation of biofilm by *Hafnia alvei* isolated from raw milk is mediated by many environmental factors including presence of QS molecule acyl homoserine lactone (Vivas *et al*., 2010; Viana *et al*., 2009). Similarly, works with *Vibrio cholerae* and *Serratia liquefaciens* showed that autoinducer 2 (AI-2) is essential for biofilm formation (Hammer and Bassler, 2003). The N-acyl-homoserine lactone and *lux*I/*lux*R dependent quorum sensing regulatory system plays active role in inhibiting *Serratia plymouthica* RVH1 population (Van Houdt *et al*., 2007).

Reports for the use of QS molecules by bacteria for the formation of biofilm in food processing industry are available yet its exact molecules and their molecular mechanism needs to be elucidated. Thus it is clear that biofilm formation is a threat to the food processing industry hence blocking the QS molecules can prevent biofilm formation. Most of the studies reveal that compounds namely AI-1 and AI-2 are the most noted QS molecules that are involved in signaling between bacteria (Ammor *et al*., 2008). Many of the food spoilage compounds or enzymes like cellulase, chitinase, protease, pectate lyase, polygalacturonase, pectin lyase, lipases and nuclease are strongly under the control of QS. Hence, by blocking the cell to cell talk food spoilage can be controlled thereby improving the shelf life of the packaged foods in the food industry (Liao *et al*., 1997). Cyanidin prevents biofilm formation by *Streptococcus pyogenes* due to anti-biofilm and antiquorum sensing effect (Limsuwan and Voravuthikunchai, 2008). In *K. pneumonia* biofilm formation involves AI-2 transport genes, *lux*S dependent signal molecule and type-2 QS regulatory molecules (Xavier and Bassler, 2003). They are inhibited by *Syzygium cumini* (L.) Skeels and its derivative anthocyanin malvidin and cyaniding, by disrupting the QS communication mechanism among bacteria (Gopu *et al*., 2015). A natural compound anthocyanin-cyanidin showed QS inhibitory and anti-biofilm property against *Klebsiella pneumonia* pathogen. *In-silico* techniques confirm that at reduced sub-lethal concentration cyanidin diminish the exopolysaccharide (EPS) production to allow direct contact of bacteria with antibacterial agent and reduce the biofilm formation among *Klebsiella pneumonia* in dose dependent form by inhibiting certain QS dependent pathways (Gopu and Shetty, 2016). Similarly in another study *Capparis spinosa* also showed significant reduction in exopolysaccharide (EPS) production in *P. mirabilis* (Abraham *et al*., 2011). In concentration dependant manner rutin against *Escherichia coli* and quercetin against *Vibrio harveyi* displayed inhibition of biofilm formation (Vikram *et al*., 2010).

POTENTIAL APPLICATIONS OF QUORUM SENSING

The QS can play potent role in the control of bacterial infections by interfering with their signaling systems, so that pathogenic gene expression can be blocked. Numerous proteolytic, lipolytic, chitinolytic and pectinolytic activities associated with the deterioration of foods can be regulated by quorum sensing. In nitrogen fixation by symbiotic bacteria Rhizobium nodulation and symbiosome formation is regulated via quorum sensing molecules (Hoang *et al*., 2004). The growth of certain extremophilic bacteria surviving under extreme environmental conditions as haloalkaliphilic archeon bacteria *Natronococcus occultus* and Halomonas, hyperthermophilic *Thermotoga maritime* and acidophilic *Acidithiobacillus ferrooxidans* is also controlled through AHL signaling of QS systems (Paggi *et al*., 2003; Johnson *et al*., 2005; Llamas *et al*., 2005; Rivas *et al*., 2007). The food-borne pathogens such as *Escherichia coli* O157:H7, *Listeria monocytogenes*, *Pseudomonas fluorescens*, Bacillus, Salmonella, *Yersinia enterocolitica* and *Campylobacter jejuni* form biofilms on food surfaces and used equipment, leading to serious health problems and QS systems appear to be instrumental in all phases of biofilm formation (Williams *et al*., 2007). Milk and dairy products are easily susceptible to spoilage by psychrotrophic bacteria which implies the involvement of quorum sensing in the spoilage of milk by certain bacteria such as *Serratia* spp. *Pseudomonas* spp. which are responsible for the slime formed on the meat surfaces and spoilage of meat and meat products (Dunstall *et al*., 2005; Yang *et al*., 2009) stored under aerobic chill (3-8°C) conditions where QS through AHL signals, such as C4-HSL, 3-oxo-C6-HSL, C6-HSL, C8-HSL and C12-HSL, have been detected (Steindler and Venturi, 2007). In a study, *Serratia proteamaculans* spoiled the pasteurized milk kept at room temperature for 18 h due to lipolytic and proteolytic enzymatic activity regulated through AHL-based 3-oxo-C6-HSL mediated quorum-sensing system and if sprI gene is inactivated to produce mutant form of *Serratia proteamaculans,* strainB5a, this genetic modification abrupt the bacterial QS and prevented the milk spoilage (Christensen *et al*., 2003). If members of Enterobacteriaceae family as *Erwinia* spp. or Pseudomonas bacteria belonging to family Pseudomonadaceae are present in fruits and vegetables their high concentration spoils the texture due to pectinolytic activity of bacteria and results into spoilage of fruits and vegetables with altered tastes and off-odors. Texture breakdown due to spoilage have shown involvement of broad range of AHLs (mainly 3-oxo-C6-HSL and C6-HSL) signals of QS system. The presence of QS signaling compounds in pasteurized milk and in meat and fish products that are refrigerated, vacuum-packaged and under modified atmosphere reveals that existing preservative techniques are inadequate.

ROLE OF QUORUM-SENSING INHIBITORS IN FOOD PRESERVATION

Quorum sensing inhibitors are termed as Quorum Quenching (QQ) since these molecules confuse the bacteria while formation of biofilms (Skandamis and Nychas, 2012). It is envisioned that QS Inhibitors (QSI) are typically analogue compounds of the AHLs which can block expression of virulence without affecting growth and also decrease the risk of resistance development. A promising group of quorum-sensing inhibitors is the halogenated furanones produced by the Australian red alga, *Delisea pulchra* which interfere with the receptor proteins and release of the AHL signal. These compounds have reduced bacterial resistance to disinfectants, reduced toxin production and also inhibit expression of virulence factors (Flodgaard *et al*., 2005). Treatment with these analogue compounds reduced the expression of AHL-regulated virulence factor and adversely affects the generation and development of biofilm. Although, QSI molecules offer a promising alternative but some disadvantages like unstability, toxic nature to human and also to rainbow trout are hurdles that prevent its uses in food processing industry (Rasch *et al*., 2004; Lynch and Wiener-Kronisha, 2008).

The bioactive dietary phytochemical extracts from fruits, vegetables, plant sources and spice radically inhibited quorum sensing. Several plants and its extract like carrot, crown vetch, tomato, soybean, habanero garlic, water lily, garlic, bean sprouts, chamomile, natural compounds, essential oils such as ascorbic acid and cinnamaldehyde were found to inhibit bacterial growth. Vanilla extract and natural furocoumarins from grapefruit juice may also be used as novel quorum-sensing inhibitor (Rasmussen *et al*., 2005; Choo *et al*., 2006; Mihalik *et al*., 2007; Khan *et al*., 2009; Vikram *et al*., 2010). Glycosyl flavonoids obtained from *Cecropia pachystachya* Trécul and *Capparis spinosa* are potential source of quorum sensing inhibitor molecules (Abraham *et al*., 2011; Brango-Vanegas *et al*., 2014). Cinnamaldehyde and derivative compounds of cinnamaldehyde decrease the virulence of *Vibrio* spp. by regulating the quorum sensing through *lux*R (Brackman *et al*., 2008). The virulence of *Pseudomonas aeruginosa* PAO1 can be reduced by using eugenol and ellagic acid derivatives obtained from *Terminalia chebula* Retz as these compounds are capable of down regulating the genetic expression of quorum sensing genes in *Pseudomonas aeruginosa* (Sarabhai *et al*., 2013; Zhou *et al*., 2013). Aspirin is another quorum sensing inhibitor molecule against *Pseudomonas aeruginosa* (El-Mowafy *et al*., 2014). Garlic contains several QSI compounds and one of them is acyclic disulfur which is a potent antagonist of QS based on *lux*R (Skandamis and Nychas, 2012). Ginger, a member of Zingiberaceae family also inhibited quorum sensing in pathogenic bacteria through its phenolic derivatives zingerone and gingerol (Kumar *et al*., 2014). Study demonstrated that orange extract containing O-glycosylated flavanones viz naringin, neohesperidin and hesperidin minimize and inhibit the production of QS mediators produced by *Y. enterocolitica* and *Chromobacterium violaceum* along with reducing the formation of biofilm (Truchado *et al*., 2012). Recent study reports that *Amomum tsaoko* (Black Cardamom) has QSI property. At a concentration of 4 mg mL^{-1} extracts from *Amomum tsaoko* showed maximum QSI property against *S. Typhimurium* (Rahman *et al*., 2015). Quorum-sensing inhibitor compounds can reduce the adherence and growth of pathogens in the food items, production of harmful metabolic toxin and proliferation of food-related bacteria. Use of natural or synthetic quorum-sensing inhibitors is an imperative idea to adapt them in food industry through pharmaceutical intervention and pave the way for their application in novel food preservation techniques. Understanding the mechanism of quorum-sensing systems in food ecosystems can help in addressing the problem of food spoilage and quorum sensing inhibitors can be verified and promoted as food preservatives to enhance food safety and so the consumers health.

CONCLUSION

Increasing antibiotic resistance among the pathogenic bacteria is a documented daunting dilemma as bacteria evolve escape strategies against traditional antibacterial agents and conventional techniques. Cell-to-cell communication (quorum sensing) between various bacterial pathogens is a population dependent phenomenon used by bacteria for regulating broad range of activities including adaptation to the changing environmental conditions during growth for their better survival and characteristic expression of phenotypes by coordinated gene regulation. The production and secretion of small, diffusible signal molecules during bacterial growth are labeled as autoinducers and N-acyl homoserine lactones (AHLs) which command the QS by modulating the gene expression in bacteria. The concentration of these signal molecules increase with the growing population in the environment and when it attains a threshold or quorum level desired beneficial phenotypic effects are produced by regulation and control of quorum-sensing-dependent target gene expression. As no external stimuli is involved in bacterial cell talk hence, phenomenon is referred as autoinduction. The various processes modulated by quorum sensing are chiefly concerned with the regulation of virulence, determination of bacterial pathogenicity, development of genetic competence, transfer of conjugative plasmids, sporulation, biofilm formation, antimicrobial peptide synthesis, food spoilage and symbiosis for their survival under adverse environmental conditions. Therefore, disrupting the QS signaling pathway by interfering QS mechanism through quorum sensing inhibitors would be a novel strategy against bacterial pathogens without giving rise to the development of antibiotic resistance.

Much research is presented in the literature but still result and application oriented further studies are desired to unveil the comprehensive mechanism of anti QS and anti-biofilm action of QSI against variety of bacterial pathogens. The identification and characterization of anti-QS compounds (QSI) as new antipathogenic and antibacterial candidates might play important role in reducing the virulence and pathogenicity of bacteria including even drug-resistant bacteria, in reducing the biofilm hazard for safe infection-free health and in combating the food-borne pathogens for safe food production. This review would help in understanding the concept and promoting the applications of quorum sensing for exploring the role of signaling molecules and potential of QS inhibitors by pharmaceutical and biotechnological interventions to use them as food bio-preservatives to prevent the food spoilage and economic loss to the health industries.

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