Review Article

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Dentistry Section

Role of Quorum-sensing Inhibitors in Managing Oral Biofilms: A Narrative Review

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ABSTRACT

One of the most robust microbial ecosystems in the human body is found in oral biofilms. These biofilms create serious difficulties in the treatment of periodontal disease, dental caries, and peri-implant diseases. Traditional antimicrobial approaches often fail due to the intrinsic resistance of biofilm communities and their ability to evade host defenses. Quorum Sensing (QS) is a regulatory system that responds to bacterial cell population density, virulence factor expression, and modulates gene expression. Oral biofilms on dental implants and tooth surfaces can be disrupted using advanced QS-based strategies. A complex bacterial communication system, i.e., QS lets oral bacteria coordinate their activities, including biofilm development. Through chemical signals, bacteria sense and respond to population density, controlling gene expression, producing biofilm growth, and higher pathogenicity. One interesting approach to stop biofilm generation and lower pathogenicity is disrupting QS signalling pathways. The addition of Quorum Sensing Inhibitors (QSI) to tooth surface biofilms and biofilms related to dental implants has lately attracted much attention in studies. Recent advances in nanotechnology, including nanoparticle- and microparticle-mediated QSI delivery, present innovative solutions for sustained release and surface functionalisation of dental implants, thereby preventing colonisation at its earliest stages. The emergence of QSI-based treatments has the potential to solve the worldwide concern of antibiotic resistance while simultaneously improving treatment outcomes. This review will deal with the current understanding of QS mechanisms in oral biofilms and the strategies to manage the oral biofilms using QS inhibition.

Keywords: Antibacterial agents, Biofilm, Drug resistance, Signal transduction

INTRODUCTION

Microorganisms that are present at or below the gingival margin are the source of inflammatory periodontal diseases. Although these infections share numerous characteristics with other infectious diseases, they possess distinctive characteristics that are conferred by the environment in which they reside and the site of colonisation [1]. Structured microbial communities known as oral biofilms develop on tooth surfaces, having a major effect on oral health and playing a role in several pathologies. Dental caries and periodontitis can result from the dysbiosis of these biofilms, which are made up of bacteria, fungi, and other microorganisms [2]. Complex microbial interactions result from the nutrient-rich environment of the oral cavity, which promotes the development of biofilms [3]. Complex, organised colonies of bacteria are important for both oral health and disease. These biofilms have distinct characteristics that add to their pathogenicity and persistence. They may grow on a variety of oral cavity surfaces, such as teeth and mucosal membranes [4].

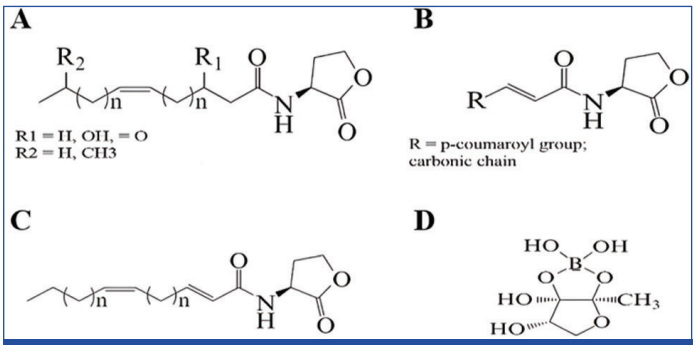
The significant features of biofilms include their structural organisation, matrix composition, QS mechanisms, and antimicrobial resistance capabilities [5]. It is widely recognised that the proliferation of microorganisms in biofilms can augment their resistance to antimicrobial treatments. This may result from less antibiotic penetration, reduced growth rates of biofilm cells, and/or lower metabolism of bacterial cells within biofilms. This resistance arises primarily from restricted antibiotic penetration, heterogeneous bacterial growth rates, and reduced metabolic activity within biofilms. Moreover, the existence of persistent cells and the expression of certain resistance genes in biofilms may enhance this tolerance. Consequently, antimicrobial treatment frequently fails to eliminate biofilms at the infection site. Hence, there is a necessity for unique anti-biofilm agents that possess fresh targets and mechanisms of action [6]. This review provides an overview of QSI and their potential applications against bacterial infections.

Mechanism of biofilm formation by Quorum Sensing (QS): It is a method of bacterial intercellular communication that includes the synthesis, detection, and reaction to extracellular signalling molecules known as Autoinducers (AI). AI increases in the environment as bacterial population density escalates, and bacteria utilise this knowledge to monitor fluctuations in their cell counts and collectively modify gene expression [7]. Numerous distinctive properties, including motility, toxin production, and biofilm formation are regulated by QS. In their individual condition, bacteria are vulnerable to the host's immunological response and the effects of antibiotics. In biofilm form, host immune cells and antibacterial agents have significant challenges in eradicating them. The substantial quantities of antibiotics are required to combat the bacteria in biofilm form. The formation of these biofilms is regulated by QS signals [8].

QS in bacteria entails the control of particular gene expression by the buildup of signalling molecules that facilitate intercellular communication [9]. It is reliant upon cell density. In minimal cellular populations, signalling compounds may be synthesised at minimal quantities; nevertheless, autoinduction results in elevated concentrations when cell density escalates. Upon reaching a certain concentration of signalling molecules (the quorum cell density), gene expression is initiated. The elevated cell densities in biofilms create an optimal environment for QS, as even minimal microcolonies (<10 cells) may trigger gene activation due to the accumulation of signalling chemicals inside the microcolony, which remain intact and undeterred. This provides unique characteristics to biofilms [10].

The QS may be categorised into four distinct phases: 1) Intracellular generation of signalling molecules; 2) secretion of these molecules, either actively or passively; 3) recognition of the signalling molecule and its binding to an inducer; and 4) activation of gene transcription [10]. QS systems in bacteria are typically categorised into a minimum of three classes: (1) LuxI/LuxR-type QS in gram-negative bacteria, utilising Acyl-Homoserine Lactones (AHL) as signalling molecules;

(2) oligopeptide-two-component-type QS in gram-positive bacteria, employing small peptides as signalling molecules; and (3) LuxS-encoded AI-2 QS present in both gram-negative and gram-positive bacteria [Table/Fig-1] [11,12].



[Table/Fig-1]: Structures of some Quorum Sensing (QS) inhibitors. Acyl-Homoserine Lactone group AHLs (A, B, C), AI-2 (AI-2, furanosyl borate diester) (D) (Courtesy- Nourhan G Naga [12]).

Quorum-Sensing Inhibitors (QSI) and their mechanism: The QSI offer a potential approach to address biofilm-associated infections. By interfering with bacterial communication, these inhibitors can significantly diminish biofilm formation and improve the effectiveness of current antibiotic therapies. These compounds represent a novel class of antibacterial agents with potential applications in managing biofilm-associated infections. Due to the numerous bacteria that utilise QS to regulate virulence, QS is an innovative target for targeted therapeutic development [13]. Natural QSIs comprise plant-derived chemicals, such as furanones and flavonoids, which have demonstrated the ability to block QS in several bacterial species [14]. Synthetic QSIs, engineered to replicate or inhibit AI signalling molecules, provide a more precise strategy and have been shown to inhibit biofilm formation, diminish virulence factor synthesis, and augment the efficacy of drugs against resistant bacteria [15].

Multiple ways to disrupt bacterial QS circuits are feasible, including: (a) the suppression of AHL signal production; (b) the inhibition of AHL signal transmission; and (c) the inhibition of AHL signal the receipt [16]. Among the several options, the enzymatic degradation of QS signal molecules (AHLs) has been the most recognised and utilised. QS-regulated gene expression is crucial for biofilm formation. QS regulates the expression of genes associated with adhesion, extracellular matrix synthesis, and pathogenicity [17]. Comprehending the temporal and geographical expression patterns of these genes elucidates the stages of biofilm development, from initial attachment to full biofilm formation, facilitating the identification of crucial intervention locations for biofilm disruption [18].

a) **Quorum Sensing Inhibitors (QSI) for gram-negative bacteria**

Gram-negative bacteria often employ LuxI/LuxR-type and AI-2 QS systems [11,19]. Enzymes, including acylase, lactonase, and oxidoreductases, can preferentially inactivate AHL in gram-negative bacteria, preventing AHL buildup in the extracellular environment and inhibiting the expression of QS-regulated genes [20].

b) **Quorum Sensing Inhibitors (QSI) for gram-positive bacteria**

Precursor-derived peptides are used as AI by gram-positive bacteria. Gram-positive bacteria employ two mechanisms in QS. They are as follows: 1) A dual-component signal transduction system; 2) Internalisation [8]. This method employs oligopeptides as signalling molecules, detectable by two-component sensory proteins, which eventually influence gene expression [17].

In the oral cavity, enzymes originating from the host or produced by commensal bacteria may contribute to the degradation of AI, hence suppressing QS in harmful bacteria. Synthetic or natural analogues of AI can competitively bind to QS receptors, inhibiting the QS pathway without activation. The dynamic environment of the oral cavity, characterised by pH variations, saliva flow, and the presence of antimicrobial peptides, might affect the stability and efficacy of AIs, resulting in their inactivation [21,22].

Scope for therapeutic use: Now-a-days, a lot of health-related sectors utilise QS-inhibiting substances. Furthermore, they can be employed to treat bacterial infections as antibiotic accelerators [14]. The bacteria that are most commonly found in areas where periodontitis is active have been investigated to see how their QS systems can affect a variety of host and bacterial activities [23]. In general, QS inhibitory drugs work by focusing on downstream regulatory factors, QS signalling molecules, and the receptors associated with them to regulate the production of biofilms. Instead of killing bacteria or preventing their development, they alter the virulence factor expression and limit the building of biofilms, which minimises the pressure on bacterial survival and lowers drug resistance. These QSI must be delivered effectively. Surface coating with the help of microparticles infused with QSIs is one of the many strategies that have been considered and used to screen their validity [24]. Nanoparticles that seem to be effective QSI and have recently gained attention for oral cavity biofilms and other applications are also of great interest [25]. The available evidence on QSI in oral pathogens, along with corresponding study types, targets, is shown in [Table/Fig-2] [22,26-30].

Author	Study type	Target organisms	Key findings
Muras A et al., (2020) [22]	In-vitro	Oral biofilms (periodontal isolates)	Detected AHL-lactonase Aii20J significantly inhibited oral biofilm formation in different *in-vitro* biofilm models.
Asahi Y et al., (2010) [26]	In-vitro	*P. gingivalis*	Modified AHL analogues inhibited biofilm; thinner, less organised structures observed
Ryu EJ et al., (2016) [27]	In-vitro	*F. nucleatum, P. gingivalis, T. forsythia*; *A. actinomycetemcomitans* coaggregation	D-galactose blocked AI-2 activity, reduced biofilms, and inhibited coaggregation
Kaspar JR et al., (2021) [28]	In-vitro	*S. mutans* with commensal streptococci	Commensals suppressed *S. mutans* peptide QS signalling, showing interspecies modulation
Cho YJ et al., (2016) [29]	Animal study (murine)	*P. gingivalis*	Combination of brominated furanone + D-ribose reduced alveolar bone loss and suppressed *P. gingivalis*
Amara B et al., (2018) [30]	Animal study (murine)	Mixed-infection periodontitis model	QSIs (a furanone compound and D-ribose) attenuated periodontal breakdown, reduced alveolar bone loss

[Table/Fig-2]: Key studies on Quorum-Sensing Inhibitors (QSI) in oral pathogens [22,26-30].

CONCLUSION(S)

The prospects of QSI for the management of oral biofilms are encouraging, especially in tackling issues related to dental implants and periodontal diseases. Small molecules similar to those implicated in QS are being considered as crucial modulators of pathogenic behaviors and significant contributors to biofilm formation in bacteria. Consequently, techniques designed to manipulate small-molecule regulation of bacterial behaviours are currently seen as very promising. The advancement of dental implants coated with QSIs may inhibit biofilm formation, hence improving implant success rates. These innovative anti-biofilm technologies may ultimately result in therapeutics that outperform existing antibiotic treatments.

REFERENCES

[1] Socransky SS, Haffajee AD. Dental biofilms: Difficult therapeutic targets. *Periodontol 2000*. 2002;28:12-55.

[2] Marsh PD, Zaura E. Dental biofilm: Ecological interactions in health and disease. *J Clin Periodontol*. 2017;44(Suppl 18):S12-S22.
[3] Karygianni L, Ren Z, Koo H, Thurnheer T. Biofilm matrixome: Extracellular components in structured microbial communities. *Trends Microbiol*. 2020;28(8):668-81.
[4] Bowen WH, Burne RA, Wu H, Koo H. Oral biofilms: Pathogens, matrix, and polymicrobial interactions in microenvironments. *Trends Microbiol*. 2018;26(3):229-42.
[5] Flemming HC, Wingender J, Szewzyk U, Steinberg P, Rice SA, Kjelleberg S. Biofilms: An emergent form of bacterial life. *Nat Rev Microbiol*. 2016;14(9):563-75.
[6] Fux CA, Costerton JW, Stewart PS, Stoodley P. Survival strategies of infectious biofilms. *Trends Microbiol*. 2005;13(1):34-40.
[7] Papenfort K, Bassler BL. Quorum sensing signal-response systems in Gram-negative bacteria. *Nat Rev Microbiol*. 2016;14(9):576-88.
[8] Yada S, Kamalesh B, Sonwane S, Guptha I, Swetha RK. Quorum sensing inhibition, relevance to periodontics. *J Int Oral Health*. 2015;7(1):67-69.
[9] Miller MB, Bassler BL. Quorum sensing in bacteria. *Annu Rev Microbiol*. 2001;55:165-99.
[10] Plančak D, Musić L, Puhar I. Quorum sensing of periodontal pathogens. *Acta Stomatol Croat*. 2015;49(3):234-41.
[11] Basavaraju M, Sisnity VS, Palaparthy R, Addanki PK. Quorum quenching: Signal jamming in dental plaque biofilms. *J Dent Sci*. 2016;11(4):349-52.
[12] Naga NG, Shaaban MI, El-Metwally MM. An insight on the powerful of bacterial quorum sensing inhibition. *Eur J Clin Microbiol Infect Dis*. 2024;43(11):2071-81.
[13] Hartman G, Wise R. Quorum sensing: Potential means of treating gram-negative infections? *Lancet*. 1998;351(9106):848-49.
[14] Zhou L, Zhang Y, Ge Y, Zhu X, Pan J. Regulatory mechanisms and promising applications of quorum sensing-inhibiting agents in control of bacterial biofilm formation. *Front Microbiol*. 2020;11:589640.
[15] Vashistha A, Sharma N, Nanaji Y, Kumar D, Singh G, Barnwal RP, et al. Quorum sensing inhibitors as therapeutics: Bacterial biofilm inhibition. *Bioorg Chem*. 2023;136:106551.
[16] Hentzer M, Givskov M. Pharmacological inhibition of quorum sensing for the treatment of chronic bacterial infections. *J Clin Invest*. 2003;112(9):1300-07.
[17] Kalia VC, Raju SC, Purohit HJ. Genomic analysis reveals versatile organisms for quorum quenching enzymes: Acyl-homoserine lactone-acylase and -lactonase. *Open Microbiol J*. 2011;5:1-13.
[18] Sionov RV, Steinberg D. Targeting the Holy Triangle of quorum sensing, biofilm formation, and antibiotic resistance in pathogenic bacteria. *Microorganisms*. 2022;10(6):1239.
[19] Rutherford ST, Bassler BL. Bacterial quorum sensing: Its role in virulence and possibilities for its control. *Cold Spring Harb Perspect Med*. 2012;2(11):a012427.
[20] Chen F, Gao Y, Chen X, Yu Z, Li X. Quorum quenching enzymes and their application in degrading signal molecules to block quorum sensing-dependent infection. *Int J Mol Sci*. 2013;14(9):17477-500.
[21] Koo H, Allan RN, Howlin RP, Stoodley P, Hall-Stoodley L. Targeting microbial biofilms: Current and prospective therapeutic strategies. *Nat Rev Microbiol*. 2017;15(12):740-55.
[22] Muras A, Otero-Casal P, Blanc V, Otero A. Acyl homoserine lactone-mediated quorum sensing in the oral cavity: A paradigm revisited. *Sci Rep*. 2020;10(1):9800.
[23] Polizzi A, Donzella M, Nicolosi G, Santonocito S, Pesce P, Isola G. Drugs for the quorum sensing inhibition of oral biofilm: New frontiers and insights in the treatment of periodontitis. *Pharmaceutics*. 2022;14(12):2740.
[24] Kang M, Kim S, Kim H, Song Y, Jung D, Kang S, et al. Calcium-binding polymer-coated poly(lactide-co-glycolide) microparticles for sustained release of quorum sensing inhibitors to prevent biofilm formation on hydroxyapatite surfaces. *ACS Appl Mater Interfaces*. 2019;11(8):7686-94.
[25] Hemmati F, Rezaee MA, Ebrahimzadeh S, Yousefi L, Nouri R, Kafil HS, et al. Novel strategies to combat bacterial biofilms. *Mol Biotechnol*. 2021;63(7):569-86.
[26] Asahi Y, Noiri Y, Igarashi J, Asai H, Suga H, Ebisu S. Effects of N-acyl homoserine lactone analogues on *Porphyromonas gingivalis* biofilm formation. *J Periodontal Res*. 2010;45(2):255-61.
[27] Ryu EJ, Sim J, Sim J, Lee J, Choi BK. D-Galactose as an autoinducer 2 inhibitor to control the biofilm formation of periodontopathogens. *J Microbiol*. 2016;54(9):632-37.
[28] Kaspar JR, Lee K, Richard B, Walker AR, Burne RA. Direct interactions with commensal streptococci modify intercellular communication behaviors of *Streptococcus mutans*. *ISME J*. 2021;15(2):473-88.
[29] Cho YJ, Song HY, Ben Amara H, Choi BK, Eunju R, Cho YA, et al. In vivo inhibition of *Porphyromonas gingivalis* growth and prevention of periodontitis with quorum-sensing inhibitors. *J Periodontol*. 2016;87(9):1075-82.
[30] Ben Amara H, Song HY, Ryu E, Park JS, Schwarz F, Kim BM, et al. Effects of quorum-sensing inhibition on experimental periodontitis induced by mixed infection in mice. *Eur J Oral Sci*. 2018;126(6):449-57.

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