

Quorum Quenching Potential of Autoinducer Ssp(A4K-A11K) in Inhibiting Streptococcus mutans Biofilm Formation

by Perpustakaan IIK Bhakti Wiyata

Submission date: 14-Sep-2025 10:38AM (UTC+0700)

Submission ID: 2501132344

File name: WJARR-2024-3255_2_-_Sawitri_Dwi_Indah_Pertami_IIK_BW.pdf (788.52K)

Word count: 2563

Character count: 13664

Quorum Quenching Potential of Autoinducer Ssp(A4K-A11K) in Inhibiting *Streptococcus mutans* Biofilm Formation

Devy Ratriana Amiati *, Nur Dianawati, Ernita Sari, Endah Kusumastuti and Sawitri Dwi Indah Pertami

Department of Oral Biology, Faculty of Dental Medicine, Bhakti Wiyata Institute of Health Sciences, Kediri, Indonesia.

World Journal of Advanced Research and Reviews, 2024, 24(01), 2606–2610

Publication history: Received on 17 September 2024; revised on 24 October 2024; accepted on 26 October 2024.

Article DOI: <https://doi.org/10.30574/wjarr.2024.24.1.3255>

Abstract

Background: *Streptococcus mutans* (*S. mutans*) is a normal flora of the human oral cavity that develops and forms biofilms. *S. mutans* biofilm can be a problem in the oral cavity and can be a serious problem in systemic health. Autoinducer Ssp(A4K-A11K) is an autoinducer synthesized by the quorum sensing system of *Streptococcus gordonii* (*S. gordonii*) which has the ability to inhibit the formation of *S. mutans* biofilm. This inhibition mechanism is known as quorum quenching.

Objective: To determine the quorum quenching mechanism of autoinducer Ssp(A4K-A11K) in inhibiting *S. mutans* biofilm formation.

Methods: Article searches using 3 databases namely Pubmed, Science direct, and ProQuest were screened according to inclusion and exclusion criteria.

Results: Autoinducer Ssp(A4K-A11K) is an amino acid with positively charged residues on the α -helix that can inhibit the attachment of *S. mutans* to the tooth surface and inhibit the formation of the *S. mutans* Biofilm eDNA structure. In addition, autoinducer Ssp(A4K-A11K) is able to suppress the adhesion of *S. mutans* by inhibiting the interaction between AgI/II (from *S. mutans* bacteria) with glycoprotein-340 and hydroxyapatite in the teeth.

Conclusion: Autoinducer Ssp(A4K-A11K) is able to inhibit *S. mutans* biofilm formation and could be one of the future antibiofilm and anti-caries therapies.

Keywords: Quorum quenching; Ssp(A4K-A11K); Biofilm; *Streptococcus mutans*

1. Introduction

S. mutans is a facultative gram-positive bacterium that lives in the human oral cavity and has the ability to metabolize various carbohydrates into organic acids (acidogenicity). *S. mutans* can form biofilms and survive under very low pH conditions (aciduric) (1). Biofilm is a cluster of microorganisms that are tightly attached to each other and embedded in a matrix of Extracellular Polymeric Substances (EPS) (2). EPS consists of polysaccharides, proteins, lipids, and nucleic acids (DNA and RNA) that play a role in the virulence process, and genetic transfer (3,4,5).

One of the diseases caused by the presence of *S. mutans* biofilm is dental caries. Dental caries is defined as a disease of the hard tissues of the teeth (6). Caries occurs when bacteria, salivary glycoproteins and glucans adhere to the tooth surface. If this condition is allowed to gradually decrease the pH of the tooth surface, and will dissolve tooth enamel (demineralization) (6,7). In some cases dental caries can be a serious problem for general health. One of the problems

* Corresponding author: Devy Ratriana Amiati

that arise is the presence of systemic infections that occur when bacteria in caries enter the bloodstream and cause infections in other organs (systemic) (8).

Quorum quenching is one way to inhibit *S. mutans* biofilm formation. Quorum quenching is defined as a mechanism of inhibiting bacterial communication using chemicals or enzymes (9). The mechanism of quorum quenching can be executed through inhibition of the synthesis of signal molecules/inducers present in biofilms, through direct signal degradation, inhibition of the attachment of signal molecules to receptors, and analog delivery of receptor signal molecules, and inhibition of signal transduction cascade (10). Ssp(A4K-A11K) is part of the SspA/B (antigen family proteins I/II) of *S. gordonii* that has the ability to bind *S. gordonii* to other bacteria and also aids attachment to salivary glycoproteins that coat the teeth (11). Ssp(A4K-A11K) is composed of α -helical peptides that contain many positively charged amino acids (12)

This review article aims to review the potential of quorum quenching autoinducer Ssp(A4K-A11K) in inhibiting *S. mutans* biofilm formation.

14 2. Material and methods

2.1. Study Design

This review article written using narrative review study design. Three database using in this review article are Pubmed, Science direct, and ProQuest

2.1.1. Inclusion Criteria

- Artikel published within 2004-2024
- Article written using English language
- Article are full-text

2.1.2. Exclusion Criteria

- The article is not in accordance with the topic of the review
- Article published more than the last 20 year
- Article use languages other than English and Indonesian

3. Results and discussion

3.1. Biofilm *S. mutans*

S. mutans biofilm is a group of *Streptococcus bacteria* that adhere to each other's surfaces and are embedded in a self-produced matrix that is an extracellular polymer matrix (2). *S. mutans* biofilms form through a series of processes involving Competence-Stimulating Peptide (CSP) and ComX-inducing peptide (XIP), which regulate biofilm maturation, acid tolerance, oxidative stress, and bacteriocin production (13). CSP is regulate the production of Glycosyltransferases (GTF) enzymes by catabolizing sucrose to produce glucans that contribute to the build-up of extracellular matrix polysaccharides (EPS). GTFs also function as architectural designers to form biofilm structures, mediating adherence to tooth enamel and bacterial (1). *S. mutans* produces three glucosyltransferases (GTFs) including gtf-B, gtf-C and gtf-D (14).

The gtfB and gtfC genes encode enzymes responsible for the synthesis of insoluble glucans, which is a major characteristic of *S. mutans*. The glucan synthesized by GtfB is responsible for microcolony formation, while the glucan synthesized by GtfC by attaching cells and microcolonies to the surface of the substratum (15). SpaP/P1/Pac is one of the most studied adhesins and results in the synthesis of the dual antigen Agl/II (1). SpaP is upregulated by the VicK gene to form Agl/II dual antigen synthesis for attachment and sucrose-independent biofilm formation (16).

3.2. Synthesis of Autoinducer Ssp(A4K-A11K)

The synthesis of the autoinducer Ssp(A4K-A11K) originates from the quorum sensing of the bacterium *S. gordonii*, LuxS, which expresses cell wall proteins, including surface proteins SspA, SspB, collagen binding domain protein (CbdA), and serine-rich repeat (SRR) glycoproteins, such as gordonii surface protein B (GspB) and Hs antigen (Hsa) for attachment to the surface (17,18). SspA/B then stimulates the formation of autoinducer Ssp(A4K-A11K) which *S. gordonii* uses for

adhesion to the tooth surface and saliva to form biofilm (11). Autoinducer Ssp(A4K-A11K) is composed of the substitution of K (lysine) for A (alanine) at position 4 and position 11 in the consensus sequence (DYQAKLAAYQAEI) of the SspA/B peptide (26).

Autoinducer Ssp(A4K-A11K) has the highest binding to salivary component activity and SRCRP2 compared to several SspA/B peptide analogs. SspA/B can interact with salivary components including lysozyme, soluble immunoglobulin A, amylase, proline-rich proteins, and salivary agglutinins. Autoinducer Ssp(A4K-A11K) is more specific, and more stable in inhibiting *S. mutans* biofilm formation than SspA/B origin (19).

3.3. Interaction of autoinducer Ssp(A4K-A11K) and *S. mutans* Biofilms

Research conducted by Koba et al. on *S. mutans* treated with autoinducer Ssp(A4K-A11K) with concentrations of 0.125, 0.25, 0.375, 0.5, 0.625, and 0.75 Mm decreased in biofilm formation (19). Another study conducted by Ito et al. on *S. mutans* grown in 96-well microplate, then treated with autoinducer Ssp(A4K-A11K) 100 µl obtained a decrease in *S. mutans* biofilm formation (20). Both studies concluded that the antibiofilm activity of autoinducer Ssp(A4K-A11K) occurs due to reduced adherence of *S. mutans* to saliva. Autoinducer Ssp(A4K-A11K) can inhibit the attachment of *S. mutans* to the tooth surface because, they compete for adhesion to salivary components including lysozyme, amylase, and proline-rich proteins that play a role in biofilm formation (20). Autoinducer Ssp(A4K-A11K) can inhibit *S. mutans* biofilm formation on saliva-coated hydroxyapatite surfaces (19). Bady et al. mentioned that autoinducer Ssp(A4K-A11K) works to inhibit *S. mutans* biofilm formation by blocking the interaction between AgI/II and salivary pellicle on the tooth surface (21).

The content of positively charged amino acids in the autoinducer Ssp(A4K-A11K) also contributes to inhibiting the formation of *S. mutans* biofilm. Research conducted by Koba et al. states that Ssp(A4K-A11K) is an amino acid with positively charged residues on the α-helix that can inhibit *S. mutans* attachment to the tooth surface (19). Other studies that complement these studies mention that amino acids are able to damage mature biofilms and inhibit the rate of cell attachment due to decreased planktonic cell viability. Fluorescence and confocal results obtained a decrease in eDNA in bacteria treated with amino acids (22).

eDNA in the biofilm formation process functions in the formation and initial attachment of bacteria to the tooth surface. Reduced eDNA or the inability of bacteria to form eDNA structures can be interpreted as a failure of bacteria to build a biofilm foundation. This inhibits biofilm maturation, which in turn inhibits its growth (23, 22). In addition, the low number of viable cells in the biofilm may be due to the inability of the cells to attach and aggregate, resulting in a reduced biofilm (CFU/ml) (22).

Autoinducer Ssp(A4K-A11K) also has the ability to suppress the adhesion of *S. mutans* by inhibiting the interaction between AgI/II (from *S. mutans* bacteria) with glycoprotein-340 and hydroxyapatite present on the teeth (12; 21; 24; 25). In another study conducted by Ito mentioned that autoinducer Ssp(A4K-A11K) cannot kill *S. mutans*, but works directly by suppressing adhesion which is the starting point of biofilm formation (12).

4. Conclusion

Autoinducer Ssp(A4K-A11K) is able to inhibit *S. mutans* biofilm formation and could be one of the future antibiofilm and anti-caries therapies.

Compliance with ethical standards

Disclosure of conflict of interest

All authors of this work declare that there are no conflicts of interests concerning this paper publication.

References

- [1] Lemos J.A., S.R. Palmer, L. Zeng, Z.T. Wen, J.K. Kajfasz, I.A. Freires, J. Abranches and L.J. Brady. The Biology of *Streptococcus mutans*. Microbiology spectrum. 2019; 7(1): 1-12
- [2] Vestby, L. K., Grønseth, T., Simm, R., & Nesse, L. L. Bacterial Biofilm and its Role in the Pathogenesis of Disease. Antibiotics. 2020; 9(2): 59

- [3] Ebert, C., Tuchscher, L., Unger, N., Pöllath, C., Frederike Gladigau, Popp, J., Löffler, B. and Neugebauer, U. Correlation of crystal violet biofilm test results of *Staphylococcus aureus* clinical isolates with Raman spectroscopic read-out. *Journal of Raman Spectroscopy*. 2021; 52(12): 2660-2670
- [4] Jamal, M., Ahmad, W., Andleeb, S., Jalil, F., Imran, M., Nawaz, M. A., Hussain, T., Ali, M., Rafiq, M., & Kamil, M. A. Bacterial biofilm and associated infections. *Journal of the Chinese Medical Association*. 2018; 81(1): 7-11.
- [5] Merritt, J., & Qi, F. The mutacins of *Streptococcus mutans*: regulation and ecology. *Molecular Oral Microbiology*. 2011; 27(2): 57-69
- [6] Jyoti, N.P.C.P., Giri, P.R.K., Handoko, S.A., Kurniati, D.P.Y., & Rahaswati L.W.A. Hubungan tingkat pengetahuan dan perilaku ibu dalam merawat gigi anak terhadap kejadian karies anak di TK Titi Dharma Denpasar. *Bali Dental Jurnal*. 2019; 3(2): 1-10.
- [7] Lin, Y., Chen, J., Zhou, X., & Li, Y. Inhibition of *Streptococcus mutans* biofilm formation by strategies targeting the metabolism of exopolysaccharides. *Critical Reviews in Microbiology*. 2021; 47(5): 667-677
- [8] Santika, T.I., Yuniarti, & Astuti, R.D.I. Tingkat Pengetahuan Penyebaran Infeksi dan Manifestasi Sistemik Karies Gigi Mahasiswa Kedokteran Unisba. *Prosiding Pendidikan Dokter*. 2015: 616-620
- [9] Sikdar, R., & Elias, M. Quorum quenching enzymes and their effects on virulence, biofilm, and microbiomes: a review of recent advances. *Expert Review of Anti-Infective Therapy*. 2020; 18(12): 1221-1233
- [10] Brackman, G., & Coenye, T. Quorum Sensing Inhibitors as Anti-Biofilm Agents. *Current Pharmaceutical Design*. 2014; 21(1): 5-11
- [11] Zhang Y., Yu L., Angela N., Ali K., & Mark C.H. Inactivation of *Streptococcus gordonii* SspAB Alters Expression of Multiple Adhesin Genes. *American society for microbiology*. 2005; 73(6): 1-12
- [12] Ito T. Streptococcal SspA/B Analogue Peptide Inhibits *Streptococcus mutans* Biofilm Via Antagonistic Mechanism. *Journal Pediatric Dentistry*. 2019; 57(1):1-6.
- [13] Shields, R. C., & Burne, R. A. Growth of *Streptococcus mutans* in Biofilms Alters Peptide Signaling at the Sub-population Level. *Frontiers in Microbiology*. 2016; 7: 1075
- [14] Nam, Y.J., & Hwang, Y.S. Antibacterial and antioxidant effect of ethanol extracts of *Terminalia chebula* on *Streptococcus mutans*. *Clinical and Experimental Dental Research*. 2021; 7(6): 987-994
- [15] Xiao, J., Klein, M. I., Falsetta, M. L., Lu, B., Delahunty, C. M., Yates, J. R., & Koo, H. The Exopolysaccharide Matrix Modulates the Interaction between 3D Architecture and Virulence of a Mixed-Species Oral Biofilm. *PLoS Pathogens*. 2012; 8(4): 1-17.
- [16] Shanmugam, K., Sarveswari, H. B., Udayashankar, A., Swamy, S. S., Pudipeddi, A., Shanmugam, T., & Neelakantan, P. Guardian genes ensuring subsistence of oral *Streptococcus mutans*. *Critical Reviews in Microbiology*. 2020; 46(4): 1-17
- [17] Bathla, S. *Textbook of Periodontics*. 2th ed. London: Jaypee Brothers Medical; 2017. p. 79-80
- [18] Andrian, E., Qi, G., Wang, J., Halperin, S. A., & Lee, S. F. Role of surface proteins SspA and SspB of *Streptococcus gordonii* in innate immunity. *Microbiology*. 2012; 158(2): 2099-2106
- [19] Koba, H., Okuda, K., Watanabe, H., Tagami, J., & Senpuku, H. Role of lysine in interaction between surface protein peptides of *Streptococcus gordonii* and agglutinin peptide. *Oral Microbiol Immunol*. 2009; 24(2): 162-169
- [20] Ito, T., Takahiro, I., & Takehiko, S. Streptococcal adhesin SspA/B analogue peptide inhibits adherence and impacts biofilm formation of *Streptococcus mutans*. *PLoS ONE*. 2017; 12(4): 1-15.
- [21] Brady, L. J., Maddocks, S. E., Larson, M. R., Forsgren, N., Persson, K., Deivanayagam, C. C., & Jenkinson, H. F. The changing faces of *Streptococcus* antigen I/II polypeptide family adhesins. *Molecular Microbiology*. 2010; 77(2): 276-286
- [22] Warraich, A.A., Mohammed, A.R., Perrie, Y., Hussain, M., Gibson, H., & Rahman, A. Evaluation of anti-biofilm activity of acidic amino acids and synergy with ciprofloxacin on *Staphylococcus aureus* biofilms. *Scientific Reports*. 2020; 10(1): 1-10
- [23] Das, T., Sharma, P. K., Busscher, H. J., van der Mei, H. C. & Krom, B. P. Role of extracellular DNA in initial bacterial adhesion and surface aggregation. *Appl Environ Microbiol*. 2010; 76(10): 3405-3408

- [24] Ito, T., Ichinosawa, T., Ito, I.N., Watanabe, C., & Shimizu, T. Streptococcal SspB Peptide Analog Inhibits. *Open Journal of Stomatology*. 2016; 6(3): 81-89
- [25] Zhang, O.I., Niu, Y.J., Yu, O.Y., Mei, L.M., Jakubovic, S.N., & Chu, H.C. 'Peptide Designs for Use in Caries Management: A Systematic Review. *J. Mol. Sci.* 2023; 24(4): 4247
- [26] Cheng R.P., Girinath P., & Ahnad R. Effect of lysine side chain length on intra-helical glutamate lysine ion pairing interactions. *Biochimistey*. 2007; 46(37): 10528-10537

Quorum Quenching Potential of Autoinducer Ssp(A4K-A11K) in Inhibiting Streptococcus mutans Biofilm Formation

ORIGINALITY REPORT

12%	5%	11%	%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

- 1

Anika Ogemdi Chinwend. "METAGENOMICS IN-SIGHT INTO THE MICROBIAL STRUCTURAL DIVERSITY OF ANAEROBIC DIGESTER UTILISING FRUIT WASTE AS SUBSTRATE", Journal of Microbiology, Biotechnology and Food Sciences, 2020

Publication

1%
- 2

João Oliveira, Hugo Proença. "Chapter 10 Caries Detection in Panoramic Dental X-ray Images", Springer Science and Business Media LLC, 2011

Publication

1%
- 3

Mhatre, Eisha, Ramses Gallegos Monterrosa, and Ákos T. Kovács. "From environmental signals to regulators: Modulation of biofilm development in Gram-positive bacteria : Environmental signals for Gram-positive biofilm", Journal of Basic Microbiology, 2014.

Publication

1%
- 4

Decker, Eva-Maria, Christian Klein, Dimitri Schwindt, and Christiane von Ohle. "Metabolic activity of Streptococcus mutans biofilms and gene expression during exposure to xylitol and sucrose", International Journal of Oral Science, 2014.

Publication

1%
- 5

biblio.ugent.be

Internet Source

1%

6	Ying Liu, Xiangyu Zhang, Yuzhi Wang, Feifei Chen, Zhifen Yu, Li Wang, Shuanglu Chen, Maoding Guo. "Effect of citrus lemon oil on growth and adherence of <i>Streptococcus mutans</i> ", <i>World Journal of Microbiology and Biotechnology</i> , 2013 Publication	1 %
7	wiredspace.wits.ac.za Internet Source	1 %
8	Robert C. Shields, Greg O'Brien, Natalie Maricic, Alexandria Kesterson et al. " Genome-Wide Screens Reveal New Gene Products That Influence Genetic Competence in ", <i>Journal of Bacteriology</i> , 2017 Publication	1 %
9	Tatsuro Ito, Hidenobu Senpuku, Takahiro Ichinosawa, Nana Ikematsu-Ito, Nao Kimura, Takehiko Shimizu. "SspB Peptide Assay Reveals Saliva-Mediated <i>Porphyromonas gingivalis</i> Attachment", <i>Open Journal of Stomatology</i> , 2015 Publication	1 %
10	Xiao-Yang Liu, Shuxia Guo, Anuradha Ramoji, Thomas Bocklitz, Petra Rösch, Jürgen Popp, Han-Qing Yu. "Spatiotemporal Organization of Biofilm Matrix Revealed by Confocal Raman Mapping Integrated with Non-negative Matrix Factorization Analysis", <i>Analytical Chemistry</i> , 2019 Publication	1 %
11	insights.ovid.com Internet Source	1 %
12	Huihui Liu, Lingyu Wang, Zhixiong Xie, Ping Shen. "Involvement of DNA in biofilm	<1 %

formation II: From bacterial adhesion to
biofilm formation", Wuhan University Journal
of Natural Sciences, 2012

Publication

-
- 13 M. Kawashima. "Real-time interaction of oral streptococci with human salivary components", Oral Microbiology and Immunology, 8/2003

Publication

-
- 14 Muthmainah, Hanik Badriyah Hidayati, Budi Yanti. "Improving Health for Better Future Life: Strengthening from Basic Science to Clinical Research", CRC Press, 2023

Publication

-
- 15 Thongchai Taechowisan. "Streptomyces sp. ST8 extracts attenuate growth, acid production, adhesion, biofilm formation, and water-insoluble glucan synthesis of Streptococcus mutans", Microbial Ecology in Health and Disease, 2008

Publication

-
- 16 pubmed.ncbi.nlm.nih.gov

Internet Source

-
- 17 Das, Theerthankar, Shama Sehar, and Mike Manefield. "The roles of extracellular DNA in the structural integrity of EPS and bacterial biofilm development", Environmental Microbiology Reports, 2013.

Publication

-
- 18 Louisa J. Stewart, Youngjin Hong, Isabel R. Holmes, Samantha J. Firth et al. "Salivary Antimicrobial Peptide Histatin-5 Does Not Display Zn(II)-Dependent or -Independent Activity against Streptococci", ACS Infectious Diseases, 2023

19

"Molecular Principles of Adhesion and Biofilm Formation", Springer Series on Biofilms, 2015.

Publication

<1 %

20

Hyeon-Hee Yu. "*Asarum sieboldii* Extracts Attenuate Growth, Acid Production, Adhesion, and Water-Insoluble Glucan Synthesis of *Streptococcus mutans*", Journal of Medicinal Food, 12/2006

Publication

<1 %

21

Ruby May A. Sullan, James K. Li, Paula J. Crowley, L. Jeannine Brady, Yves F. Dufrêne. "Binding Forces of P1 Adhesin ", ACS Nano, 2015

Publication

<1 %

22

T. Hamada, M. Kawashima, H. Watanabe, J. Tagami, H. Senpuku. "Molecular Interactions of Surface Protein Peptides of *Streptococcus gordonii* with Human Salivary Components", Infection and Immunity, 2004

Publication

<1 %

Exclude quotes On

Exclude matches Off

Exclude bibliography On

Quorum Quenching Potential of Autoinducer Ssp(A4K-A11K) in Inhibiting Streptococcus mutans Biofilm Formation

GRADEMARK REPORT

FINAL GRADE

GENERAL COMMENTS

/100

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5