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Review ARTICLE

Oral Pathogens and Their Antibiotics from Marine Organisms: A Systematic Review of New Drugs for Novel Drug Targets

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Background: Recent studies have elucidated the quorum-sensing mechanisms, biofilm formation, inter-pathogen interactions, and genes related to oral pathogens. This review aims to explore the recent expansion of drug targets against oral pathogens and summarize the current research on novel antibiotic substances derived from marine organisms that target oral pathogens.

Methods: A comprehensive literature review summarized the novel mechanisms pertaining to quorum-sensing signal transmission systems, biofilm formation, and metabolite exchange in oral pathogens. The amino acid sequences of the 16 proteins identified as potential drug targets were systematically classified and compared across various oral microorganisms.

Results: Through a literature review, we identified nine studies researching quorum sensing signaling inhibitors targeting oral pathogens. A comparison of the amino acid sequences of 16 potential drug targets in oral microorganisms revealed significant differences between oral pathogens and beneficial oral symbiotic microorganisms. These findings imply that it is possible to design drugs that can bind more selectively to oral pathogens.

Conclusion: By summarizing the results of recent research on the signaling mechanisms that cause pathogenicity, new drug targets against oral pathogens were proposed. Additionally, the current status of developing new antibiotics for oral pathogens using recently developed quorum sensing inhibitors and natural products derived from marine organisms was introduced. Consequently, marine natural products can be used to develop drugs targeting new proteins in oral pathogens.

Key Words: Antibiotics, Biofilms, Marine organisms, Oral pathogen, Quorum sensing

Introduction

1. Background

The human oral cavity contains a complex community of microorganisms (including oral pathogens) that exert a substantial influence on dental and systemic health. Various microbial niches appear in the tissues of the human oral cavity owing to factors such as nutritional content, pH, oxygen concentration, and metabolic properties of the microbial ecosystem[1-3]. Biofilm formation in the oral environment is a critical mechanism for these oral pathogens. While biofilms naturally occur in healthy teeth, the accumulation of successive dental biofilms can play a critical role in the development of diseases, such as dental caries, gingivitis, and periodontitis[4,5]. Furthermore, bacteria from dental biofilms may cause systemic diseases such as endocarditis, diabetes mellitus, atherosclerosis, rheumatoid arthritis, and orodigestive cancer through bacteremia or indirect manners[6-10]. Research on oral pathogens is important to understand their roles in various systemic diseases

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and conditions. Poor oral hygiene and periodontal health can affect systemic health and vice versa[11]. Understanding the relationship between oral pathogens and systemic diseases can improve diagnosis, prevention, and treatment strategies. Therefore, research on oral pathogens is crucial to improve overall oral and systemic health outcomes.

Oral biofilms are formed in several stages and involve various bacteria. Saccharolytic bacteria, such as *Streptococcus, Lactobacillus*, and *Actinomyces* species, are prominent in the formation of dental caries by creating acids that erode tooth enamel[1,12]. Various organisms living in the oral cavity, including these species, are known oral pathogens. Proteolytic bacteria such as *Prevotella* and *Porphyromonas* species break down proteins into amino acids and further degrade these amino acids, generating short-chain fatty acids, ammonia, sulfur compounds, and indole/skatole, which serve as virulent factors contributing to periodontitis and oral malodor[13,14]. *Porphyromonas gingivalis* is a common cause of chronic periodontitis and an indicator of disease progression[15,16]. It affects the proliferation of oral tumor cells and modifies epidermal growth factor receptor signaling, which is relevant to the development of oral tumors and colorectal cancer. They play key roles in the formation of multispecies dental biofilms[17]. Gram-negative bacteria such as *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* are the main cause of infections, ranging from pneumonia to bloodstream infections, and their presence in the oral cavity can lead to systemic and opportunistic infections (Fig. 1)[18].

Additionally, other species and types of oral pathogens live in the human oral cavity. For example, *Candida albicans* is a fungus that contributes to oral infections, particularly in immunocompromised individuals[19,20]. *Aggregatibacter actinomycetemcomitans*, *Filifactor alocis*, *Staphylococcus aureus*, *Aspergillus fumigatus*, *Mucor*, *Cryptococcus*, *Corynebacterium*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, and *Neisseria* species are well-known oral pathogens[21-24].

These bacteria rapidly colonize various surfaces within the oral tissue despite the turbulent environment within the human oral cavity. Colonization begins within several minutes and extensive microbial deposition occurs within a few hours. Biofilm development in the oral cavity can be divided into adhesion/coaggregation, microbial interactions, and extracellular matrix formation stages[25,26]. *Streptococci* participated in all stages, and a wide variety of bacteria participated in each stage (Table 1). Oral streptococci express numerous adhesins on their cell surface. Adhesins are key elements that allow streptococci to anchor to human tissues and other bacterial cells[27]. Oral streptococci, including commensal, cariogenic, and extraoral streptococci, express a family of proteins called antigens I/II (AgI/II). AgI/II allows streptococci to attach to enamel surfaces and aggregate with other bacteria by binding to the salivary agglutinin glycoprotein gp340[28,29].

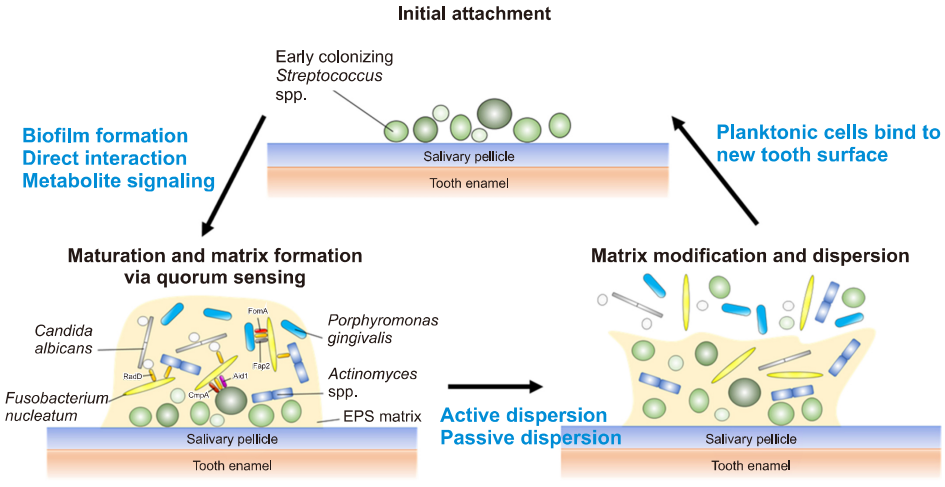

Fig. 1. Stages of oral biofilm formation and dispersion. Several oral pathogens use quorum-sensing signaling to form biofilms. Additionally, direct interactions with other pathogens or signaling using secondary metabolites occur. Biofilm dispersion can be largely divided into active dispersion by signals of the microorganism itself and passive dispersion by external physical stimulation. EPS: extracellular polymeric substances.

Table 1. Representative Examples of Participating Bacteria throughout the Oral Biofilm Formation Stages

Adhesion/coaggregation		Interaction		Matrix production	
Pathogen	Description	Pathogen	Description	Pathogen	Description
Streptococci	AgI/II proteins result in aggregation	Early colonizing streptococci	Produce acids from sugars	*Streptococcus mutans*	Produce insoluble glucans, an important component of biofilm matrix
Porphyromonas gingivalis	Bindto pre-existing *Streptococcus gordonii* biofilm	*Aggregatibacter actinomycetemcomitans*	Utilize lactate produced by streptococci	*Enterococcus faecalis*	Forma structural biofilm scaffold with proteins and extracellular DNA
Fusobacterium nucleatum	Coaggregate with almost all other oral bacteria	*Veillonella* sp.	Participate in numerous mutualistic interactions	*Neisseria meningitides*	

2. Objectives

This review introduces the recent studies on the various pathogenic mechanisms of oral pathogens. Specifically, we describe the direct interactions between pathogens, quorum sensing signaling, and metabolite exchange that occur during biofilm formation by oral pathogens. We also summarized the virulence factors involved in biofilm formation by oral pathogens. These newly identified mechanisms of pathogenic virulence factors may provide new drug targets for the development of novel antibiotics against oral pathogens. Furthermore, we suggested methods for selective drug development against specific oral pathogens through a sequence comparison of drug target proteins that have not been previously introduced. Additionally, we present the possibility of discovering new antibacterial substances in marine organisms based on recent successful findings.

Materials and Methods

1. Literature and protein sequence database search

A literature search was performed using PubMed (https://pubmed.ncbi.nlm.nih.gov/) and Google Scholar (https://scholar.google.com/) databases. The Basic Local Alignment Search Tool (BLAST) was used to identify homologous protein sequences in other species.

2. Protein sequence identity and similarity calculation

Sixteen well-known drug target proteins for general pathogens were selected through a literature review using PubMed and Google Scholar. The sequences of these 16 proteins from the pathogen *P. gingivalis* were retrieved from the UniProt Knowledge Base (UniProtKB) protein sequence database. Using the 16 protein sequences from *P. gingivalis* as queries, homologous proteins from other oral microorganisms were searched in the UniProtKB protein sequence database. The search results were compiled by one researcher and subsequently reviewed by two authors who were not involved in the initial search process. Protein sequence alignments and analyses were performed using the web-based multiple alignment program ClustalW (https://www. genome. jp/tools-bin/clustalW).

Results and Discussion

1. The demand to develop new antibiotics

Antibiotics prescribed for oral health are commonly used in dentistry for periodontal infections, non-periodontal infections, localized infections, focal infections, and as preventive measures during dental procedures. Antibiotic treatment involves direct application at the site of infection or systemic administration via ingestion. It is crucial to choose an appropriate approach by targeting antibiotic therapy specifically for oral pathogens, while preserving beneficial oral commensal bacteria, thereby inhibiting the growth of oral pathogens[30,31].

Overuse and misuse of antibiotics in odontogenic infections can promote the colonization of resistant bacteria, and antibiotic-resistant gene-containing plasmids can spread

across a broad niche of bacteria through transmission[30,31]. The emergence of multidrug-resistant oral pathogens that render conventional treatments ineffective has become a critical global health concern since conventional treatments become ineffective[32]. The development of novel antimicrobial agents is crucial owing to the increasing threat of multidrug-resistant oral pathogens and limited options for therapy[33,34]. Therefore, it is important to identify valuable sources of antibiotics in natural ecosystems[35-37].

2. Interpreting recent studies

Marine organisms are rich sources of antibiotics. Marine sponges, such as those from the phylum Porifera, produce bioactive compounds that can be used to improve human health[38]. Natural compounds derived from marine microorganisms (including bacteria, fungi, actinomycetes, and cyanobacteria) exhibit promising antimicrobial properties and can act against various antibiotic-resistant pathogenic strains. Antibiotics produced by bacteria living in marine environments have also been studied; diverse metabolites have been isolated and their chemical structures elucidated[39]. Actinomycetes (specifically, marine actinomycetes) have been identified as potential producers of novel antibiotics, with strains such as *Streptomyces sampsonii*, *Streptomyces halstedii*, and *Nocardiopsis alba* showing significant antibiotic activity against various pathogens[40,41]. Additionally, marine-derived natural products have been explored for their anti-biofilm activity, and 129 marine-derived natural products and their synthetic analogs have been reviewed for their effectiveness in combating biofilm formation (Table 2)[42].

Biologically active compounds have been identified in several brown algae species. Fucoidan is a long chain, sulfated, fucose-rich polysaccharide found in the cell walls of brown macroalgal species, including *Fucus vesiculosus*, *Cladosiphon okamuranus*, *Laminaria japonica*, and *Undaria pinnatifida*[43]. It is widely studied owing to its diverse pharmacological effects (including antitumor effects) that promote the apoptosis of cancer cells[44-46], as well as its antiviral, anti-inflammatory, anti-allergic, and hypotensive effects[44].

Microbial symbionts in marine sponges and corals produce bioactive compounds with antimicrobial properties. Halistanol sulfate, discovered in the sponge *Halichondria moori,* exhibits antibacterial activity against *Streptococcus mutans,* which is the main etiological agent of human dental caries[47,48]. Halistanol sulfate A exhibited the strongest antibacterial effect against *S. mutans*, inhibits biofilm formation in planktonic cells, and reduces the expression of

Table 2. Antimicrobial Substances against Oral Pathogens Derived from Marine Organisms

Natural compound	Source	Description	Reference
Fucoidan	*Fucus vesiculosus, Cladosiphon okamuranus, Laminaria japonica,* and many other brown macroalgal species	・Long chain sulfated and fucose-rich polysaccharide. ・Broad pharmacological effects include antibacterial, antiviral, and anti-inflammatory effects. ・Antimicrobial activity against *Candida albicans*, *Streptococcus mutans*, and *Porphyromonas gingivalis*.	43～46
Halistanol sulfate	*Halichondria moori* from marine sponge	・Inhibition of biofilm formation and reduction of biofilm-associated gene expression in *S. mutans* and *Streptococcus sanguinis*.	47, 48
Mayamycin	*Streptomyces* sp. HB202 bacteria isolated from marine sponge	・Inhibitory effect against *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus*.	49
Salinisporamycin	*Salinispora* sp. marine bacteria from bottom sediments	・Inhibition of adenocarcinoma cell growth. ・Antimicrobial activity against *S. aureus* and *C. albicans*.	50
Fridamycin A/D	*Streptomyces* marine bacteria from bottom sediments	・Antibacterial activity against multidrug-resistant *S. aureus*.	51
Callinectin	*Callinectes sapidus* from blue crab	・Antibacterial activity against Gram-negative bacteria.	53
Coumarin	Diverse group of algae, marine fungi, and ascidians	・Inhibition of biofilm formation of *P. gingivalis* through reducing AI-2 activity.	54, 55

biofilm-related genes (gtfB, gtfC, and gbpB)[47,48]. Halistanol sulfate A also inhibits *Streptococcus sanguinis* at higher concentrations[47]. Mayamycin is an aromatic polyketide identified in a symbiotic *Streptomyces* sp. strain isolated from the marine sponge *Halichondria panicea*. It has shown significant pharmacological activities, including cytotoxicity against human cancer cell lines and antimicrobial activity against various bacteria such as *P. aeruginosa* and methicillin-resistant *S. aureus*[49]. Marine sediment bacteria produce diverse compounds with potential antibiotic properties. For example, salinisporamycin, a rifamycin antibiotic isolated from the marine actinomycete *Salinispora arenicola*, inhibits the growth of human lung adenocarcinoma cells and exhibits antimicrobial activity against *P. aeruginosa*

Table 3. Amino Acid Sequence Differences of Drug Development Target Protein in Various Oral Bacteria

Possible drug target protein in *Porphyromonas gingivalis* (UniProtKB code)	Sequence identity/homology (UniProtKB code) with homologous protein				
	Streptococcus mutans	*Fusobacterium nucleatum*	*Enterococcus faecalis*	*Neisseria meningitidis*	*Streptococcus salivarius*
Methionine-tRNA ligase (Q7MXK7)	35.29%/53.07% (A0A829BNI5)	34.14%/52.15% (Q8RE57)	34.13%/52.38% (Q837B3)	36.38%/55.29% (Q9K1Q0)	37.32%/53.09% (J7SIB3)
Peptide deformylase (Q7MT07)	29.36%/45.96% (Q8DWC2)	39.41%/60.10% (Q8REF0)	30.80%/44.64% (Q82ZJ0)	37.13%/53.96% (P63916)	28.28%/43.85% (J7TGU5)
Methionine Aminopeptidase (A0A134DR99)	38.89%/54.25% (Q8DT38)	47.08%/66.42% (A0A0X3Y2E4)	41.94%/58.78% (A0A3N3SAK1)	43.17%/61.15% (A0A0H5QGA8)	37.99%/54.22% (J7TU94)
Beta-ketoacyl-[acyl-carrier-protein] synthase III (Q7MAV3)	38.53%/60.91% (Q8DSN2)	43.63%/59.49% (Q8RGX7)	38.04%/54.08% (Q820T1)	39.83%/57.66% (Q9JXR6)	40.51%/59.21% (J7SIA1)
DNA gyrase subunit A (Q8L3L7)	47.77%/67.08% (A0A0E3VYF0)	47.53%/67.15% (A0A0M4SCH3)	49.72%/69.97% (A0A1J6YID4)	44.82%/62.87% (A0A076U4V3)	48.54%/68.61% (A0A6N2YRL6)
DNA gyrase subunit B (A0A134DMA2)	55.57%/71.92% (A0A829BP53)	53.77%/70.61% (A0A101K4X9)	56.05%/70.85% (Q839Z1)	40.93%/55.13% (A0A0H5QAZ0)	56.33%/72.58% (A0A7L6WLW5)
DNA topoisomerase IV subunit A (A0A2D2N546)	27.48%/43.98% (A0A829BMX9)	N/A	28.63%/45.78% (Q93HU6)	28.35%/43.60% (A0A0H5QAL8)	29.65%/45.79% (J7TQR1)
DnaK (P0C937)	60.73%/72.36% (O06942)	60.00%/71.82% (Q8RH05)	60.78%/73.45% (Q835R7)	60.39%/73.69% (Q9K0N4)	61.40%/73.10% (J7TPQ1)
Peptidoglycan glycosyltransferase (A0A2D2NAU4)	27.65%/40.93% (A0A829BJP3)	26.50%/44.43% (A0A133P5Z8)	26.62%/40.80% (Q9EXN1)	29.61%/44.90% (A9M1V1)	27.81%/40.92% (J7TPX1)
1-Deoxy-D-xylulose-5 -phosphate reductoisomerase (Q7MUW3)	N/A	42.11%/62.44% (Q8R622)	N/A	45.15%/63.35% (Q9K1G8)	N/A
Superoxide dismutase [Mn/Fe] (P19665)	41.59%/54.67% (P09738)	N/A	45.41%/57.49% (Q838I4)	N/A	41.63%/54.55% (A0A0A1DUC0)
Aspartate semialdehyde dehydrogenase (A0A2D2N2E1)	46.60%/61.52% (P10539)	30.81%/46.70% (A0A3P1VYK2)	45.95%/62.16% (A0A2S7M0C8)	32.93%/49.39% (P30903)	44.33%/61.34% (J7TZ02)
Methylenetetrahydrofolate dehydrogenase/cyclohydrolase (Q7MVE9)	47.40%/64.29% (Q8DVC1)	40.51%/61.41% (Q8RDM4)	46.36%/68.21% (Q836W7)	47.27%/63.02% (P0C277)	45.37%/63.58% (J7TX79)
Riboflavin biosynthesis protein (Q7MWK9)	N/A	53.10%/68.57% (A0A101K6I4)	51.43%/66.90% (R3HR06)	N/A	N/A
Lumazine synthase (Q7MUR5)	N/A	41.32%/60.48% (Q8RIR4)	34.91%/57.99% (R3K342)	37.02%/51.93% (P66037)	N/A
FAD synthetase (A0A2D2N1C2)	36.08%/54.26% (A0A829BS71)	33.24%/52.91% (A0A0M4SS57)	33.71%/52.81% (A0A3N3ZCW2)	36.52%/54.78% (A0A2X1VAD0)	35.90%/54.70% (A0A428B2K5)

N/A means the sequence information is not available in the database.

and *C. albicans*[50]. Similarly, Fridamycin A and Fridamycin D, identified in a *Streptomyces* sp. strain from the marine sediment of the Philippine archipelago, exhibit antibacterial activity against multidrug-resistant *S. aureus*[51]. Additionally, a *Pseudomonas* sp. associated with the soft coral *Sinularia polydactyla* shows antibacterial activity against *Streptococcus equi* subspecies, although the specific antibacterial substance remains unidentified[52].

Potential antibiotic candidates are found not only in bacteria but also in various marine organisms. For example, blue crabs (*Callinectes sapidus*) synthesize the antimicrobial peptide called callinectin in their hemolymph, which is effective against gram-negative bacteria[53]. Coumarins, isolated from a diverse group of marine organisms, including algae, fungi, and ascidians, also show antimicrobial activity[54]. Notably, coumarin has the potential to act as a quorum-sensing inhibitor by inhibiting the AI-2 activity of *P. gingivalis*[55]. Oroidin is a secondary metabolite of the marine sponge *Agelas conifera* that significantly reduces *P. gingivalis* biovolume[56]. These compounds reduced the expression of mfa1 and fimA in *P. gingivalis*, which encode the minor and major fimbrial subunits, respectively. These fimbrial adhesins are necessary for the co-adhesion between *P. gingivalis* and *Streptococcus gordonii*. These results demonstrate the potential of a small molecule inhibitor-based approach for preventing diseases associated with *P. gingivalis*[56]. Neoechinulin B is a natural marine product and a promising drug candidate for allevia-

Table 4. Several Oral Pathogens have Quorum Sensing Systems

Oral pathogen	Quorum sensing molecules	Quorum sensing type	Reference
Porphyromonas gingivalis	Autoinducer-2 (AI-2)	LuxS-encoded autoinducer (AI)-2 quorum sensing	83～85
Prevotella intermedia	Autoinducer-2 (AI-2)	LuxS-encoded autoinducer (AI)-2 quorum sensing	84, 85
Fusobacterium nucleatum	Autoinducer-2 (AI-2)	LuxS-encoded autoinducer (AI)-2 quorum sensing	85, 86
Streptococcus mutans	Autoinducer peptides (AIPs) Competence-stimulating peptide (CSP)	ComD/ComE two-component-type quorum sensing	87
Aggregatibacter actinomycetemcomitans	Autoinducer-2 (AI-2)	LuxS-encoded autoinducer (AI)-2 quorum sensing	88

Table 5. Summary of Quorum Sensing Inhibitors Targeting Oral Pathogens

Quorum sensing inhibitor	Inhibition target	Mechanism of action	Reference
Coumarin	*Porphyromonas gingivalis*	Inhibiting AI-2 activity	53, 54
Furanone compound			
D-Ribose	*Fusobacterium nucleatum* *P. gingivalis* *Tannerella forsythia*	Inhibiting AI-2 activity and reducing biofilm formation	86, 89
D-Galactose	*F. nucleatum* *Vibrio harveyi* *P. gingivalis* *T. forsythia*	Preventing biofilm formation	90
D-Arabinose	*F. nucleatum* *P. gingivalis* *Streptococcus oralis*	Inhibiting AI-2 activity	91
Short-chain fattyacids (NaA, NaP, NaB, etc.)	*Streptococcus gordonii*	Suppressing *S. gordonii* biofilm formation	92
Bicyclic brominated furanones	*P. gingivalis* *F. nucleatum* *T. forsythia*	Inhibiting AI-2 activity without cytotoxicity or inflammatory response	93
Baicalein	*Staphylococcus aureus* *Streptococcus mutans*	Inhibiting biofilm formation and destruction	94
Furanone C-30	*S. mutans*	Inhibiting biofilm formation in *S. mutans* and its *lux S. mutant* strain	95

ting mortality and morbidity rates caused by drug-resistant infections[57]. Aurantoside K is a tetramic acid glycoside isolated from the Fijian marine sponge *Melophlus* that shows potent antifungal activity against wild-type and amphotericin-resistant *C. albicans*[58].

3. Comparison with previous studies: new drug targets against oral pathogenic microorganisms

Recent studies have shown that oral microorganisms coexist and balance the oral environment of a healthy person. When the oral environment deteriorates, the composition and ratio of oral microorganisms change, and pathogenic microorganisms increase[59-61]. Many oral pathogenic microorganisms are anaerobic, whereas commensal non-pathogenic oral microorganisms are often aerobic bacteria[62,63]. An attempt has been made to develop a drug specific to oral pathogens using the difference in energy metabolism pathways between aerobic and anaerobic microorganisms by developing an inhibitor of a characteristic enzyme only present in anaerobic microorganisms. For example, treatment with amixicile (an inhibitor targeting pyruvate:ferredoxin oxidoreductase) inhibits oral pathogen growth, whereas aerobic oral bacteria are unaffected[64,65]. Additionally, it is possible to develop a specific drug targeting oral pathogenic microorganisms because the amino acid sequences of drug target proteins differ between oral pathogenic and non-pathogenic oral microorganisms[66,67]. For example, there is a large sequence difference between peptide deformylases in *P. gingivalis* and *Streptococcus salivarius*, with 28.3% sequence identity and 43.9% sequence homology (Table 3). Thus, it is possible to develop a peptide deformylase inhibitor that can inhibit the growth of *P. gingivalis* without inhibiting the growth of *S. salivarius*[68].

When the number of pathogenic oral microorganisms increases, the expression of virulence factors and biofilm production is promoted through quorum sensing[69-71]. Recent studies have revealed the detailed mechanisms and functions of the genes involved in sensing oral pathogens. Biofilm formation induces antibiotic resistance in oral pathogenic microorganisms by inhibiting antibiotic penetration of antibiotics[72,73]. During biofilm formation, oral microorganisms are directly connected to each other through adhesion proteins and exchange various metabolites for signaling[74-76]. *Fusobacterium nucleatum* serves as a bridge between the early colonized microorganisms of the teeth and pathogenic microorganisms[77,78]. Following the discovery of quorum-sensing mechanisms and biofilm formation by oral pathogenic microorganisms, it is possible to develop antibacterial substances that only inhibit the growth of pathogens while preserving beneficial oral bacteria[79,80]. Substances that inhibit quorum sensing, biofilm formation, metabolite signaling, and direct interactions with oral pathogenic microorganisms are considered new drug candidates against oral pathogenic microorganisms (Table 4, 5)[53,54,81-95].

4. Conclusion and suggestion

Rapid developments in molecular biology, genome analysis, and metabolite analysis technologies have enabled the identification of novel oral disease mechanisms in oral pathogens. Various signaling molecules and interacting proteins related to biofilm formation by certain oral pathogens have been identified. Proteins involved in the production of signaling molecules and signal transduction during biofilm formation can serve as new drug targets against oral pathogens. If drugs are developed to target proteins unique to oral pathogens, it would be possible to selectively eliminate oral pathogens, while preserving beneficial oral commensal microorganisms. Establishing a rapid and accurate activity measurement method for each new drug candidate target protein is also necessary. In conclusion, it is important to study the various mechanisms of action of oral pathogens and identify new target proteins to develop novel antibiotics against oral pathogens. In this review, we investigated six successful cases of confirmed antibacterial activity against oral pathogens using marine natural products. Most studies on the antibacterial activity of natural marine products have been conducted on general rather than oral pathogens. Therefore, it is necessary to investigate the application of substances with known antibacterial activities against oral pathogens. Moreover, it is important to screen for novel antibiotics in marine organisms to address the antibiotic resistance issues associated with oral diseases.

Notes

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Ethical approval

Not applicable.

Author contributions

Conceptualization: Youn-Soo Shim and Jun Hyuck Lee. Data acquisition: Sehyeok Im. Formal analysis: Sehyeok Im. Funding: Jun Hyuck Lee. Supervision: Youn-Soo Shim and Jun Hyuck Lee. Writing-original draft: Sehyeok Im. Writing-review & editing: Youn-Soo Shim and Jun Hyuck Lee.

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Data availability

Raw data is provided by the corresponding author upon reasonable request.

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