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Dental Biofilm Formation: A Scoping Review

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ABSTRACT
Dental biofilm is a structured microbial community that adheres to the tooth surface and becomes embedded within a self-produced extracellular matrix. This matrix, rich in polysaccharides, proteins, and nucleic acids, enables microorganisms to survive environmental stresses and contributes to the onset of oral diseases such as caries and periodontitis. The purpose of this scoping review is to determine current knowledge the dental biofilm formation. The articles published from 2020 until 2025 were searched for using the keywords: "dental and biofilm and formation" in the PubMed, ScienceDirect, and Google scholar databases. Using PRISMA-Scr, existing articles were chosen based on inclusion and exclusion criteria. There were five articles found that were suitable for review. The data presented in the article vary according to the study's location, purpose, method, and samples. The major classes of extracellular polymeric substances that form the matrix are common to most biofilms and comprise carbohydrates, proteins, nucleic acids, and cell wall polymers, such as peptidoglycans and lipids. Several unique resistance mechanisms make biofilms particularly tough to manage. Biofilm bacteria employ multiple defense mechanisms, such as capsule protection, efflux pumps, membrane modifications, genetic adaptations, quorum sensing, metabolic dormancy, and stress responses, making them highly resistant to treatment and contributing to persistent infections.

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INTRODUCTION

Dental biofilm is a structured microbial community that adheres to the tooth surface and becomes embedded within a self-produced extracellular matrix. This matrix, rich in polysaccharides, proteins, and nucleic acids, enables microorganisms to survive environmental stresses and contributes to the onset of oral diseases such as caries and periodontitis (Marsh PD, 2006).

The formation of biofilm is not a random event, but a highly regulated process that unfolds through sequential stages: initial bacterial adhesion, early colonization, microbial co-aggregation, biofilm maturation, and eventual dispersion (KooH et al, 2013). Each stage is coordinated by a series of molecular signaling mechanisms that govern bacterial behavior, communication, and matrix production.

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Among the most critical regulators are quorum sensing systems, which allow bacteria to monitor their population density via chemical signals such as autoinducer-2 (AI-2) and competence-stimulating peptides (CSPs). These systems modulate the expression of genes related to virulence, genetic competence, and EPS biosynthesis (Li YH, Tian X, 2012)(Senadheera D, Cvitkovitch DG, 2008). Additionally, two-component regulatory systems like ComDE and VicRK play important roles in sensing environmental changes and modulating gene activity essential for biofilm development, including the production of glucosyltransferases (GtfB/C/D) that synthesize glucans for the biofilm matrix (Römling U, 2013).

The second messenger cyclic di-GMP is also pivotal in biofilm regulation. High intracellular levels of this molecule promote sessile growth, EPS secretion, and surface adherence, while low levels encourage motility and dispersion (Worthington RJ, 2012). These pathways, working in concert, form a regulatory network that ensures the structural stability and functional integrity of the biofilm. Understanding these molecular pathways provides valuable insight into the persistence and pathogenicity of oral biofilms The purpose of this scoping review is to determine current knowledge the dental biofilm formation.

METHODS

This study used scoping review method from January 2020 to June 2025. The preparation stage begins with research questions centered on the PCC criteria. The study population was S. mutans that survive in biofilm and during caries formation. The concept was to examine S. mutans ability to survive in biofilm and during caries formation. The research context was a cross sectional study, prospective cohort study, and randomized controlled trials articles used for this study.

A comprehensive literature search was conducted across multiple electronic databases, including PubMed, ScienceDirect, and Google Scholar databases. The research inclusion criteria, which include: articles published between 2020 and 2025 in both Indonesian and English; investigate dental biofilm formation; and articles in the form of observational and randomized controlled trials. Exclusion criteria included paid full-text articles.

RESULTS AND DISCUSSION

The study selection process is illustrated in Figure 1. Out of 889 articles identified through PubMed, ScienceDirect 37 articles and Google Scholar 180 articles were deemed eligible for further assessment. Ultimately, 186 studies met the inclusion and exclusion criteria and were included in the review.Table 1 provides an overview of the scope of research on metabolic disorders and periodontal disease.

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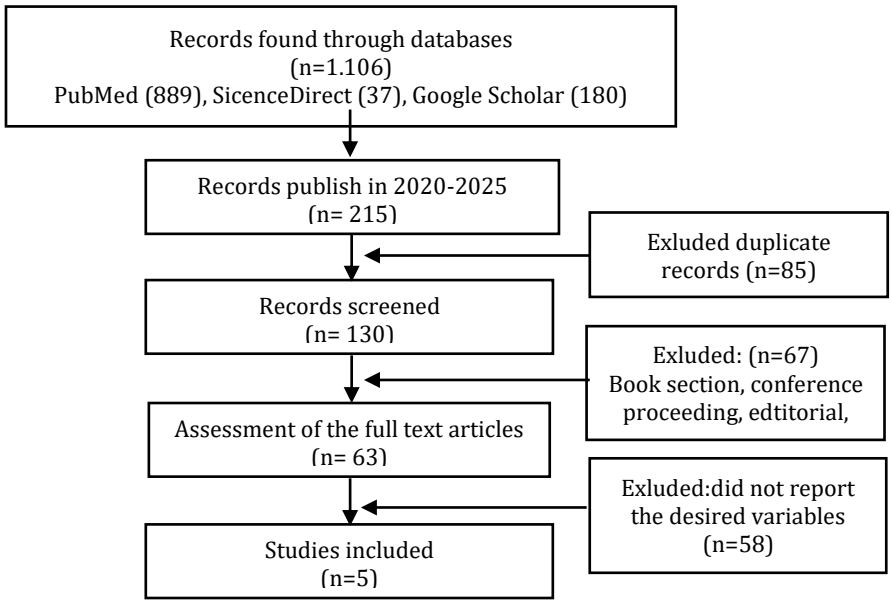

Figure 1. Research methodology

Dental biofilms, commonly known as dental plaque, are structured microbial communities that adhere to surfaces in the oral cavity. They are surrounded by an extracellular polymeric substance (EPS) that protects bacteria from environmental stress and antimicrobial agents, making them difficult to eliminate. Biofilm development stages:

1. Initial entry: Pathogenic microorganisms enter the oral cavity.
2. Adhesion: Bacteria adhere to surfaces, forming a salivary pellicle.
3. Growth: Bacteria proliferate and irreversible adhesion occurs.
4. Gene exchange: Transfer of drug-resistant genes and onset of dysbiosis.
5. Maturation: Fully mature biofilm spreads and releases multidrug-resistant bacteria.(Stetsyk MO,et al, 2020)

The dental plaque biofilm matrix

The major classes of extracellular polymeric substances that form the matrix are common to most biofilms and comprise carbohydrates, proteins, nucleic acids, and cell wall polymers, such as peptidoglycans and lipids. Carbohydrates constitute approximately 20% of the dry weight of supragingival dental plaque, and around two-thirds of these are water insoluble.[18, 19] A significant proportion of this biomass consists of intracellular storage polysaccharides and other intracellular carbohydrates.[20] In addition, approximately 2%-10% of the dry weight of dental plaque consists of glucans, which are homopolymers of glucose that are produced extracellularly from sucrose by glucosyltransferase enzymes.[19] Sucrose can also be converted to fructose polymers (fructans) by fructosyltransferases.[21] The components of the matrix are:

a. Carbohydrates: Include glucans and fructans synthesized from sucrose by oral streptococci. These contribute to adhesion but are less involved in subgingival plaque.
b. Glycoconjugates: Includes glycosylated proteins (e.g., S-layers, adhesins) that are essential for biofilm formation and structure.

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c. Capsular Polysaccharides: Influence biofilm formation and immune evasion, particularly in pathogens like *P. gingivalis*.
d. Poly-N-acetyl-D-glucosamine: A structural polysaccharide important for biofilm stability and virulence, notably in *A. actinomycetemcomitans*.
e. Teichoic/Lipoteichoic Acids: Involved in biofilm structure and intermicrobial interactions.
f. Fungal Polysaccharides: *Candida* spp. contribute mannan-glucan complexes to the matrix (Jakubovics NS, et al., 2021)

Extracellular DNA is a critical structural component of the matrix. It helps with adhesion, architecture, and defense against external threats. DNA BII proteins stabilize extracellular DNA and are conserved across bacteria, making them potential therapeutic targets.(Rostami N, et al., 2017)

Proteins include adhesins, enzymes, and amyloid proteins that contribute to biofilm architecture. Some proteins interact with eDNA, enhancing structural integrity. Proteolytic enzymes from pathogens degrade host tissues and modulate immune responses. Cell wall fragments (e.g., peptidoglycan, lipopolysaccharides) and host-derived molecules (e.g., salivary proteins, immune cell products) also integrate into the matrix. (Fong JN et.al., 2015)

Matrix components are secreted, released via vesicles, or result from cell lysis. Outer membrane vesicles play a key role in delivering DNA, proteins, and virulence factors to the matrix. Functions of the matrix are (Hobley L et al, 2015):

a. Adhesion/Cohesion: Enhances microbial attachment and biofilm mechanical stability.
b. Mass Transfer Regulation: The matrix impedes diffusion of antimicrobials and nutrients.
c. Microbial Cooperation and Competition: Matrix components mediate spatial arrangement and microbial interactions.
d. Immune Modulation: Helps bacteria evade immune responses.

Biofilm resistance mechanisms

Biofilms, including oral biofilms (dental plaque), are very difficult to treat because they protect the bacteria inside them from antibiotics and the body's immune system. Several unique resistance mechanisms make biofilms particularly tough to manage.

Capsule protection (biofilm shield). Bacteria in biofilms are covered by a thick, sticky capsule made of polysaccharides and glycoproteins. This capsule traps antibiotics, preventing them from reaching the bacteria. It also acts as a physical barrier against antimicrobial agents. Antibiotics are either neutralized by enzymes or cannot penetrate deep enough to kill the bacteria.

Cell membrane modification. Bacteria inside biofilms can change their cell membranes, reducing the number of channels (porins) where antibiotics usually enter.Antibiotics can't pass through the modified membrane. This selective barrier makes it harder for drugs to get inside bacterial cells.

Efflux pump system. Biofilm bacteria use efflux pumps to actively pump antibiotics out of their cells. Even if antibiotics manage to enter, the pumps eject them quickly. The drug concentration inside the bacteria stays too low to be effective. Plasmid and enzyme-mediated resistance. Biofilm bacteria can share plasmids (small DNA molecules) carrying resistance genes. Bacteria inside biofilms can rapidly spread resistance to multiple antibiotics. Enzymes produced by these bacteria can also destroy antibiotics.

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Genetic adaptation (mutation). Constant exposure to antibiotics encourages bacteria to mutate and adapt. Mutations can lead to the development of permanent resistance to specific antibiotics. These genetic changes can be passed on, making future treatments less effective. Quorum sensing (bacterial communication). Bacteria inside biofilms use chemical signals to communicate and coordinate their defense. They can decide as a group to form stronger biofilms or resist antibiotics more aggressively. Quorum sensing helps the biofilm grow and defend itself more efficiently.

Metabolic dormancy.Some bacteria in biofilms enter a dormant (inactive) state. Antibiotics usually target actively growing bacteria, so dormant cells can survive treatment. These sleeping cells can later "wake up" and restart the infection. Persistence cells. Persister cells are a small population of bacteria that survive antibiotic attacks without genetic resistance. They survive because they temporarily stop essential life processes targeted by antibiotics. Once the antibiotics are gone, persisters can regrow and cause chronic infections.(Singh S, et.al, 2017)

Stress response systems. Biofilm bacteria activate special genes when under stress (heat, pH changes, lack of nutrients). This helps them repair damage and survive in harsh conditions. Stress responses make bacteria even more resistant to antibiotics and immune attacks.(Rath S, et al, 2021)

Biofilm Grows Rapidly on Enamel and Composite Materials:

1. Higher Surface Roughness
    a. Enamel and composites typically have microscopic surface irregularities.
    b. Rougher surfaces provide more spaces for bacteria to attach, shelter, and accumulate.
    c. Increased surface area from roughness helps biofilm anchor more quickly.
2. Surface Energy and Hydrophilicity
    a. Enamel and composites tend to have lower surface energy and are more hydrophilic.
    b. Hydrophilic surfaces attract bacteria that thrive in moist environments.
    c. Bacteria like *Streptococcus mutans* can adhere better to these surfaces.
3. Favorable Chemical Composition
    a. Composites often contain organic resin components that bacteria can more easily colonize.
    b. Enamel, being a natural substrate, is readily recognized by oral bacteria for colonization.(Engel AS, et.al, 2020)

Why Biofilm Grows Slower and Thinner on Ceramic and Metal Alloy Surfaces:

1. Lower Surface Roughness
    a. Ceramics and metals usually have smoother surfaces after finishing and polishing.
    b. Fewer surface irregularities mean less initial bacterial attachment.
2. Surface Chemistry
    a. Metal alloys may have antibacterial ion release (like silver or copper) that can inhibit early biofilm growth.
    b. Ceramics are more chemically stable and less likely to support bacterial adhesion.

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3. Surface Energy and Charge
   a. Ceramics and metals may have higher surface energy but a surface charge that is less attractive to the negatively charged bacterial membranes.
   b. The electrostatic repulsion can make initial adhesion more difficult.
4. Pellicle Formation Differences
   On ceramics and metals, the acquired pellicle (protein layer from saliva) tends to form more slowly or less densely, delaying bacterial attachment. (Souza,et al, 2016)

CONCLUSION

The major classes of extracellular polymeric substances that form the matrix are common to most biofilms and comprise carbohydrates, proteins, nucleic acids, and cell wall polymers, such as peptidoglycans and lipids. Several unique resistance mechanisms make biofilms particularly tough to manage. Biofilm bacteria employ multiple defense mechanisms, such as capsule protection, efflux pumps, membrane modifications, genetic adaptations, quorum sensing, metabolic dormancy, and stress responses, making them highly resistant to treatment and contributing to persistent infections. The growth rate and thickness of biofilms vary by surface type, with rapid accumulation. The implications of these research are challenges in dental biofilm treatment, material selection in dentistry, importance of surface modification, potential for targeted therapies, need for personalize preventive strategies.

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