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Potential of various groups of berries as antibiofilm agents against *Streptococcus mutans,* the cause of dental caries

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Abstract

Background*:* Dental caries is a common oral disease caused by biofilm formation by *Streptococcus mutans*. This biofilm is difficult to treat with conventional medication due to the protection of the extracellular matrix that envelops the bacteria. Therefore, an effective and safe antibiofilm agent is needed as an alternative for the prevention and treatment of caries. Berries are known to contain bioactive compounds such as polyphenols, flavonoids, and tannins that have antibacterial and antibiofilm potential.

Purpose*:* Examine the potential of various groups of berries as antibiofilm agents against *Streptococcus mutans*, the cause of dental caries.

Methods: The reviewed studies include in vitro research on the antibiofilm activity of berry extracts and their bioactive compounds, as well as the molecular mechanism of action, which involves inhibiting bacterial adhesion, reducing the expression of virulence genes, and disrupting biofilm structure.

Result: Berries are significantly able to inhibit the formation of *S. mutans* biofilm, thus having the potential to be used as an active ingredient in caries prevention products such as toothpaste and mouthwash.

Conclusion: Berries are a promising natural alternative for the control of dental caries through an antibiofilm mechanism, thereby contributing to the sustainable improvement of oral health.

Keywords: Berries; Antibiofilm; *Streptococcus mutans*; Dental Caries; Polyphenols; Flavonoids

1. Introduction

Dental caries is one of the most common chronic infectious diseases worldwide and represents a significant public health problem. This disease is caused by the demineralization of hard tooth tissues, which occurs due to the metabolic activity of bacteria within the plaque biofilm on the tooth surface. One of the main bacteria involved in the formation of caries is *Streptococcus mutans*, which has a strong ability to form a tenacious biofilm on the tooth surface and produce acids that damage the enamel structure. This biofilm is a community of microorganisms organized in an extracellular polymer matrix, making the bacteria more resistant to conventional treatments such as antibiotics and antiseptics. Therefore, efforts to inhibit the formation of *S. mutans* biofilm have become one of the primary strategies in the prevention and control of dental caries [1].

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In recent years, research attention has shifted towards the use of natural agents as a safer and more environmentally friendly alternative for antibiofilm therapy. One natural source that shows great potential as an antibiofilm agent is berries. Berries, which include various groups such as strawberries, blueberries, blackberries, and raspberries, are known to be rich in bioactive compounds such as flavonoids, anthocyanins, tannins, and phenolic acids. These compounds not only possess antioxidant and anti-inflammatory activities but are also reported to have antibacterial and antibiofilm effects against various pathogenic microorganisms [6].

Research on the antibiofilm activity of berries against *S. mutans* shows promising results. The bioactive compounds in berries are thought to be capable of disrupting the process of bacterial adhesion to the tooth surface, inhibiting the formation of the biofilm matrix, and reducing acid production by *S. mutans*. The mechanism of action of these compounds is suspected to involve direct interaction with the bacterial cell wall, modification of enzymes involved in biofilm formation, and inhibition of the expression of genes that regulate bacterial virulence. This makes berries a potential candidate for the development of natural oral care products such as toothpaste, mouthwash, or nutritional supplements that can help prevent dental caries effectively and safely [3].

In addition to the advantages in terms of bioactivity, berries are also relatively easy to obtain and have a good safety profile for consumption and topical use. Various in vitro and in vivo experimental studies have investigated the antibiofilm effect of berry extracts against *S. mutans* and other microorganisms involved in oral diseases. However, the results of these studies still vary depending on the type of berry, the extraction method, the concentration of active compounds, and the assay model used. Therefore, a systematic literature review is needed to collect, evaluate, and synthesize data from various studies that have been conducted in order to provide a comprehensive overview of the potential of berries as an antibiofilm agent against *S. mutans* [4]. This literature review aims to analyze and summarize research findings related to the antibiofilm activity of several groups of berries against *S. mutans* as the primary causative bacteria of dental caries. This review is expected to provide a clearer understanding of the effectiveness of bioactive compounds in berries, the antibiofilm mechanism of action, and their potential application in the field of oral health. Furthermore, this study will also identify existing research gaps and provide recommendations for the development of further studies, particularly regarding product formulation and clinical trials [2].

The use of berries as antibiofilm agents has added value compared to conventional synthetic agents because, in addition to their therapeutic effects, berries can also provide nutritional and antioxidant benefits that support general health. With increasing bacterial resistance to antibiotics and the side effects of chemical drugs, this natural approach becomes an attractive and relevant alternative in the era of modern medicine that prioritizes the principles of safety and sustainability. Therefore, the development of berry-based antibiofilm agents has the potential to open up opportunities for innovation in oral health products that are effective, safe, and widely accepted by the public [7].

2. Research methods

This study employs a literature review method with a systematic approach to collect and analyze various research examining the antibiofilm potential of several groups of berries against *Streptococcus mutans*. Data were gathered from various primary and secondary sources, including scientific journals, articles, theses, and research reports published in both Indonesian and English. The literature search was conducted through electronic databases such as PubMed, Google Scholar, ScienceDirect, and Scopus, utilizing primary keywords such as “antibiofilm,” “berry extracts,” “*Streptococcus mutans*,” “dental caries,” and “bioactive compounds in berries.” The inclusion criteria covered studies that tested the antibiofilm activity of berries against *S. mutans* or other cariogenic bacteria, using both in vitro and in vivo experimental methods, and that were published within the last 10 years to ensure relevant and up-to-date data.

After the literature was collected, the next step involved screening the studies based on relevance, methodological quality, and the completeness of the presented data. The data obtained were then analyzed descriptively by grouping the results according to the type of berry, the bioactive compounds tested, the antibiofilm mechanism, and the effectiveness results against *S. mutans*. This analysis aimed to synthesize key findings that could provide a comprehensive overview of the potential of berries as antibiofilm agents. This study did not involve direct laboratory experiments, focusing instead on the critical interpretation of existing study results to provide recommendations for future research and the development of oral health products.

3. Results

Research concerning the potential of berries as antibiofilm agents against *Streptococcus mutans*, the primary causative bacterium of dental caries, has increasingly received attention in recent years. This is driven by the need to find effective yet safe natural treatment alternatives, considering that the excessive use of antibiotics and chemical antiseptics potentially leads to resistance and side effects on oral tissues. Based on the results of the literature review, berries and their bioactive compounds, such as polyphenols, flavonoids, and tannins, show very promising antibacterial and antibiofilm activity as preventive and control agents for caries.

Table 1 Summary of Studies on Antibiofilm Effects of Berries and Other Natural Compounds Against *Streptococcus mutans*

No	Title	Method	Results
1	Chen et al. (2020). Microbial etiology and prevention of dental caries: exploiting natural products to inhibit cariogenic biofilms.	The literature review examined various natural products that suppress caries biofilm	Natural products, such as polyphenols from berries, are effective in inhibiting the formation of *S. mutans* biofilm and reducing caries.
2	Deglovic et al. (2022). Antibacterial and antibiofilm effect of honey in the prevention of dental caries: A recent perspective.	A narrative review discussed the antibacterial and antibiofilm activities of honey.	Honey possesses significant antibiofilm activity against *S. mutans*, showing potential as a natural caries preventive agent.
3	Kováč et al. (2022). Therapeutic potential of flavonoids and tannins in management of oral infectious diseases: a review.	A systematic review on flavonoids and tannins as oral therapeutic agents.	Flavonoids and tannins from fruits and plants show strong antibacterial and antibiofilm effects on oral pathogens
4	Kranz et al. (2020). Antimicrobial effect of natural berry juices on common oral pathogenic bacteria.	In vitro experiments using berry juice against oral pathogenic bacteria.	Berry juice is capable of significantly suppressing the growth and biofilm formation of *S. mutans*.
5	Lobo et al. (2021). Compounds with Distinct Targets Present Diverse Antimicrobial and Antibiofilm Efficacy against *Candida albicans* and *Streptococcus mutans*, and Combinations of Compounds Potentiate Their Effect.	An in vitro laboratory study tested the antimicrobial effect of fruit extracts.	Fruit extracts with different components are effective against *S. mutans* and *C. albicans* biofilms through varied mechanisms.
6	Mosaddad et al. (2023). Green alternatives as antimicrobial agents in mitigating periodontal diseases: a narrative review.	A narrative review related to natural antimicrobial agents for periodontal disease.	Green agents, including polyphenols from berries, possess antibacterial and antibiofilm activity that can reduce oral pathogens.
7	Passos et al. (2021). Anticariogenic activities of *Libidibia ferrea*, gallic acid and ethyl gallate against *Streptococcus mutans* in biofilm model.	An in vitro experiment testing the antibiofilm activity of gallic acid and plant extracts.	Gallic acid and ethyl gallate significantly inhibited the formation of *S. mutans* biofilm and reduced bacterial viability.
8	Sateriale et al. (2020). Phytocompounds vs. Dental Plaque Bacteria: In vitro Effects of Myrtle and Pomegranate Polyphenolic Extracts Against Single-Species and Multispecies Oral Biofilms.	An in vitro experiment using pomegranate and myrtle polyphenol extracts	Polyphenol extracts have been shown to effectively inhibit both mono and multispecies biofilms, including *S. mutans*, through the reduction of bacterial adhesion.
9	Souissi et al. (2021). Effect of a Berry Polyphenolic Fraction on Biofilm Formation, Adherence	An in vitro study tested berry	Berry polyphenols suppressed biofilm formation, interfered

	Properties and Gene Expression of *Streptococcus mutans* and Its Biocompatibility with Oral Epithelial Cells Laboratory of Analysis, Treatment and Valorisation of Pollutants of the Environment and Products.	polyphenol fractions against biofilm and gene expression.	with bacterial adhesion, and reduced the expression of *S. mutans* virulence genes.
10	Wu et al. (2021). Beverages Containing Plant-Derived Polyphenols Inhibit Growth and Biofilm Formation of *Streptococcus mutans* and Children's Supragingival Plaque Bacteria.	An experimental study tested polyphenol-rich beverages against *S. mutans* and plaque.	Beverages with plant polyphenols significantly inhibited the growth and biofilm formation of *S. mutans* in children's dental plaque.

4. Discussion

Dental caries, as an infectious disease triggered by biofilm formation by *Streptococcus mutans*, has become a major focus of various studies examining natural-based alternatives for prevention and treatment. Of the ten journals reviewed, the majority used *in vitro* experimental methods and narrative or systematic reviews to evaluate the antibiofilm effects of various natural compounds, particularly polyphenols found in berries and other plants. Reviews on the potential of natural products and bioactive compounds such as flavonoids and tannins in inhibiting cariogenic biofilm have been presented [1,3]. This finding is consistent with results specifically showing that the juice from various types of berries was able to suppress the growth and adhesion of *S. mutans*, thus preventing the biofilm formation that underlies caries development [4].

Berry extracts are not only effective in directly inhibiting biofilm but also possess the ability to reduce the expression of bacterial virulence genes [9]. They revealed that polyphenols in berries interfere with bacterial adhesion function and reduce the bacteria's ability to form biofilm by modulating the expression of virulence-related genes. This reinforces the argument that the natural compounds in berries work via multi-mechanisms, making them potent for caries prevention. In addition to berries, other natural compounds such as gallic acid and ethyl gallate also demonstrated strong antibiofilm activity against *S. mutans* [7]. These compounds are part of the polyphenols often found in fruits and medicinal plants, supporting the hypothesis that the phenolic compound group is a promising antibacterial agent.

The practical potential of beverages and fruit extracts rich in polyphenols has been demonstrated. Their findings suggest that regular consumption or topical application of berry and polyphenol-based products can effectively inhibit *S. mutans* growth and reduce dental plaque [10], [5]. Further expanding the range of natural caries preventive agents, honey also possesses significant antibiofilm properties [2]. The importance of natural agents in managing periodontal disease, which is closely linked to oral microbiota and biofilm formation, has also been emphasized [6].

Polyphenol extracts from plants such as myrtle and pomegranate have been shown to be effective against multispecies biofilms, which is important given the usual complexity of oral biofilms [8]. This multispecies approach adds a dimension of realism and broader clinical application for natural compounds. These ten journals show consistency that bioactive compounds in berries and other plants, especially polyphenols, flavonoids, and tannins, possess effective antibiofilm activity against *Streptococcus mutans*. This effectiveness is achieved through several mechanisms, such as inhibiting bacterial adhesion, disrupting the biofilm matrix, and reducing the expression of virulence genes. The use of these natural products has the potential to be an alternative or complement in the prevention and control of dental caries, with the advantages of safety and minimal side effects.

Cariogenic biofilm formed by *S. mutans* is a key factor in caries progression [1]. This biofilm is a strongly adherent community of bacteria on the tooth surface, protected by an extracellular matrix that is difficult for drugs to penetrate. Therefore, an antibiofilm agent capable of inhibiting the formation and stability of the biofilm has high therapeutic value. Polyphenols in berries are able to reduce bacterial adhesion and disrupt the biofilm matrix formation process, thereby inhibiting caries progression from the initial stage [4], [9].

Polyphenols found in berries are also known to have a multifaceted mechanism of action, not only being bactericidal but also modulating the expression of *S. mutans* virulence genes. For example, it was shown that berry polyphenols can reduce the expression of genes involved in adhesion and biofilm formation, such as *gtfB* and *comDE,* which contribute to reducing *S. mutans*'s ability to form a strong and treatment-resistant biofilm [9]. This finding is very important because it shows that these natural ingredients not only kill bacteria but also interfere with bacterial communication within the biofilm (quorum sensing), thereby inhibiting the formation of complex biofilm structures. Furthermore, flavonoids and tannins, also contained in berries, have strong antibacterial properties through various mechanisms,

including bacterial protein binding, inhibition of important enzymes, and damage to bacterial cell membranes [3]. These compounds can also disrupt biofilm formation through direct interaction with biofilm matrix components. This is reinforced by the study results, which tested gallic acid and ethyl gallate phenolic compounds derived from flavonoids which were able to significantly reduce *S. mutans* viability and damage the biofilm structure [7]. Thus, the presence of various types of bioactive compounds in berries provides a synergistic effect that enhances their antibiofilm activity.

In vitro research also provides an overview that berry extracts or juices are not only effective against *S. mutans* in single cultures but are also capable of inhibiting biofilm growth in more complex conditions, such as the multispecies community found in children's dental plaque [4], [10]. This indicates the potential use of berries in daily oral health products, such as toothpaste, mouthwash, or functional beverages, that can reduce the risk of caries through a natural and non-invasive mechanism. Furthermore, the research reviewing honey as an antibiofilm agent adds evidence that various natural products rich in polyphenols and other bioactive compounds can provide an effective alternative in caries prevention [2]. Honey shows an effect similar to berry extracts in inhibiting *S. mutans* biofilm. This suggests that bioactive compounds with specific chemical structures, especially those that are antioxidant and anti-inflammatory, can work through similar mechanisms to inhibit bacterial growth and biofilm formation.

Although the results of this research are very promising, most studies are still *in vitro*. This is an important consideration because the biological conditions in the human mouth are highly complex, involving interactions between various types of bacteria, saliva, the immune system, and other environmental factors that can affect the effectiveness of antibiofilm compounds. Therefore, in vivo and clinical trials are needed to ensure the safety, effectiveness, and optimal dosage of using berries or their extracts in human caries prevention. In addition, the technical challenge in developing berry-based products is maintaining the stability of the active compounds during processing and storage. Polyphenol and flavonoid compounds are known to be vulnerable to degradation by heat, light, and oxygen, necessitating formulation technology that can maintain their bioactivity so that the therapeutic benefits remain optimal when used by consumers.

Berries show significant promise as a versatile antibiofilm agent in oral health, particularly as a preventive measure. Given the rise of antibiotic resistance and concerns about synthetic chemical side effects, natural, environmentally friendly ingredients with minimal adverse effects are highly desirable. Berries, being readily available and rich in bioactive compounds, can be developed into key components for caries prevention and oral health products. On the other hand, this literature review also highlights the importance of a multidisciplinary approach combining microbiology, pharmaceutical chemistry, food technology, and dentistry to optimize the development of berry-based antibiofilm agents. Future research should focus on identifying active compounds, elucidating molecular mechanisms of antibiofilm action, conducting toxicity and safety testing, and performing clinical trials to gather comprehensive scientific evidence before commercialization.

5. Conclusion

Based on the literature review conducted, it can be concluded that various groups of berries hold significant potential as antibiofilm agents against *Streptococcus mutans*, the main bacterium causing dental caries. Bioactive compounds such as polyphenols, flavonoids, and tannins contained in berries are capable of inhibiting biofilm formation and development through various mechanisms, including reduced bacterial adhesion, disruption of virulence gene expression, and destruction of the biofilm matrix structure. This antibacterial and antibiofilm activity makes berries a promising natural alternative in the prevention and control of dental caries. Although in vitro studies show high effectiveness, further research in the form of in vivo and clinical trials is still necessary to ensure the safety, optimal dosage, and effectiveness of berries within the complex biological conditions of the human oral cavity. Furthermore, the development of product formulations that can maintain the stability of the active compounds is also an important challenge. With their promising potential and benefits, berries can be developed as a base ingredient in natural, safe, and effective oral health products to help reduce the incidence of dental caries more broadly.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest.

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