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# THE INFLEUNCE OF GRAM-NEGATIVE BACTERIA ON ORAL HEALTH: A MINI REVIEW

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## ABSTRACT

The human body hosts a diverse microbial community, with Gram-negative bacteria playing a key role in oral health due to their virulence factors that contribute to tissue destruction and inflammation. The Human Microbiome Project (HMP) emphasizes the importance of understanding the oral microbiota to improve health outcomes, the oral cavity is particularly vulnerable to imbalances caused by these bacteria, leading to periodontal diseases and other oral infections. Among them, Porphyromonas gingivalis is the most harmful, producing gingipains that degrade host tissues and evade immune responses, promoting chronic inflammation. As a keystone pathogen, it drives periodontitis, causes systemic inflammation, and has been linked to cardiovascular diseases, diabetes, and adverse pregnancy outcomes. Its resilience in anaerobic conditions and ability to form biofilms make it difficult to treat, further complicating oral health management. Understanding the role of Gram-negative bacteria, particularly P. gingivalis, is essential for advancing prevention and treatment strategies in oral health.

**KEYWORDS:** Bacteria, Gram-Negative, Oral Health, Medicinal plants.

## INTRODUCTION

Health and hygiene encompass every aspect of an individual's life, including their relationship with the environment (Malsch et al., 2024). Health is a state of physical, mental, and social well-being, not simply the absence of disease, it is an integrated whole, constantly influenced by environmental factors, with oral health playing a key role in maintaining overall well-being (Reed, G. M. 2024). Good oral health contributes to physical, mental, and social satisfaction, while the ability to smile, enabled by healthy teeth, and is an important expression of joy and emotional connection (Chan et al., 2024). Maintaining

good oral health is essential for preventing both local and systemic diseases (Lipsky et al., 2024). Poor oral hygiene has been linked to a range of issues, including psychological distress, facial disfigurement, and even death, it is also a risk factor for cardiovascular diseases, kidney problems, and other systemic conditions (Niazi, P. 2024). Special attention should be given to the relationship between chronic kidney disease and periodontitis, as elevated uremia levels impair immune function, increasing vulnerability to bacterial infections (Guo et al., 2024; Yi, Z. 2024). Gram-negative bacteria, in particular, are significant contributors to many health conditions, especially due to their antimicrobial resistance (Wang et al., 2024).

The mouth, described as the window to general health, serves as a focal point for the interaction between the body and the external environment (Kettle, J., and Warren, L. 2024). It is home to a diverse microbial community, with 500-700 species of bacteria, viruses, fungi, and protozoa colonizing various surfaces (Asmatullah et al., 2020; Niazi, P. 2024; Qiao et al.,2024; Hejran et al., 2024). Good oral hygiene helps maintain a balanced microbial community dominated by beneficial bacteria, while poor oral hygiene promotes the growth of pathogenic microorganisms, disruptions in this oral ecosystem, or dysbiosis, can lead to conditions such as dental caries and periodontitis (Pandey et al., 2024). Oral diseases remain a significant public health issue, with over 269 million cases reported since 2019, particularly among older populations, who are at higher risk (World Health Organization. 2024), as well more than 514 million children worldwide suffer from dental caries, primarily in primary teeth (Heilmann, A., and Watt, R. G. 2024), accounting for 15.8% of global oral disease cases (Mikelis et al., 2024). Various risk factors, including low household income, socio-demographic conditions, poor oral hygiene habits, inadequate nutrition, and chronic systemic diseases, all contribute to the development of oral health problems, these factors should be addressed through primary healthcare to improve oral hygiene and reduce disease burden (Wadhwa et al., 2024; Gholami, E. 2024).

Studies indicate that 13-32% of bacteria isolated from patients with oral diseases produce beta-lactamase, rendering them resistant to common antibiotics like penicillin and aminopenicillins (Basic et al., 2024), resistant bacteria such as: Streptococcus mutans: A key bacterium implicated in dental caries, Streptococcus mutans is facultative anaerobic microorganism that produces lactic acid through fermentation of sugars, which contributes to tooth enamel demineralization (Oezdemir, Z. 2024). Porphyromonas gingivalis: A major pathogen associated with periodontal disease, Porphyromonas gingivalis is a gram-negative, anaerobic bacterium that plays a crucial role in the development of periodontitis by inducing inflammation and tissue destruction through its virulence factors, including proteases (Yusoff et al., 2024). Fusobacterium nucleatum: This anaerobic gram-negative bacterium is commonly found in both the oral and gastrointestinal microbiota, it is a key player in periodontal disease, where it acts as a bridge organism that facilitates the colonization of other pathogens, contributing to the progression of periodontitis (Monib et al., 2023; Liu et al., 2024). Aggregatibacter actinomycetemcomitans: Known for its association with aggressive periodontitis, Aggregatibacter actinomycetemcomitans is a gram-negative, facultative anaerobic bacterium that can produce leukotoxins, which help evade the host immune response and contribute to tissue destruction (Talapko et al., 2024). Prevotella intermedia: A gram-negative, anaerobic bacterium, Prevotella intermedia is commonly found in periodontal infections and is involved in the inflammation and breakdown of tissues in the oral cavity, often contributing to gingivitis and periodontitis (Zhang et al., 2024). Treponema denticola: A spirochete bacterium and a major component of the oral biofilm, Treponema denticola is a gram-negative, anaerobic organism linked to periodontal diseases. It is known for its motility, which allows it to invade deeper tissues in the periodontium and exacerbate inflammation (Di Spirito et al.,

2024). Tannerella forsythia: Is gram-negative, anaerobic bacterium is strongly associated with chronic periodontitis. Tannerella forsythia produces various enzymes that facilitate tissue destruction and contribute to the inflammatory process in the gums (Schäffer, C., and Andrukhov, O. 2024).

These microorganisms, either individually or as part of a polymicrobial community, contribute to a variety of oral diseases, including dental caries, gingivitis, and periodontitis, by altering the local microbial balance and promoting inflammation, tissue damage, and infection, have been identified in the oral cavity. The primary mechanism of resistance is biofilm formation, a characteristic of Gram-negative bacteria (Hosseini Hooshiar et al., 2024). Research has also shown a strong correlation between poor oral hygiene and the presence of bacterial plaque and oral diseases (Fallea et al., 2024). More than 60% of individuals with low hygiene scores were found to have bacterial oral infections, the excessive use of antibiotics is a contributing factor to antimicrobial resistance in oral bacteria. Given the widespread impact of oral health on both local and systemic health, monitoring and addressing bacterial oral conditions is essential (Maurotto et al., 2024; Chen, W. 2024; Adeghe, E. P. 2024). The relationship between oral health and systemic conditions is increasingly recognized, with over 100 systemic diseases showing oral manifestations (Uppal et al., 2024), these conditions are often more prevalent in older populations. The impact of oral health on systemic health has become a focus of medical and dental professionals alike, although the mechanisms of this relationship are still being explored (McNeil et al., 2024). Whether causal or coincidental, the link between oral and systemic health underscores the need for collaborative efforts between dentistry and medicine Table 1 (Rotaru et al., 2024; Rajasekaran et al., 2024). Improving access to both dental and medical care is crucial for early detection and treatment, ultimately benefiting overall public health. This review aims to explore the impact of Gram-negative bacteria on oral health and their broader implications for systemic conditions.

***Table 1*** *(Associations between Oral Microbiota and Disease Pathologies (Rajasekaran et al., 2024))*

| Disease | Commensals | Pathogens | Trend | Mechanisms |
|---|---|---|---|---|
| Oral Diseases | | | | |
| Dental Caries | *Lactobacillus spp.*, *Veillonella*, *Propionibacterium*, *Bifidobacterium*, *Corynebacterium*, *Capnocytophaga* | *Streptococcus mutans* | ↑ | Acidogenic bacteria release acidic by-products, inducing enamel demineralization and cavity formation; a dysbiosis-driven condition. |
| Gingivitis | *Streptococcus spp.*, *Actinomyces spp.*, *Veillonella spp.* | *Porphyromonas gingivalis*, *Treponema denticola*, *Aggregatibacter actinomycetemcomitans*, *Fusobacterium spp.*, *Prevotella intermedia* | ↑ | Bacterial biofilm accumulates on teeth surfaces, penetrating gingival tissues and eliciting inflammatory responses. |

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| Periodontitis | *Prevotella melaninogenica* | *P. gingivalis*, *T. denticola*, *T. forsythia*, *F. nucleatum ss. polymorphum*, *P. intermedia* | ↑ | Pathogens induce inflammation, oxidative stress, immune activation, and tissue destruction, with potential systemic impacts. |
| Halitosis | *Prevotella melaninogenica*, *Veillonella spp.*, *Peptostreptococcus*, *Actinomyces spp.*, *Eubacterium*, *Megasphaera*, *Selenomonas*, *Leptotrichia*, *Eikenella corrodens* | *Treponema denticola*, *P. gingivalis*, *P. endodontalis*, *Tannerella forsythia* | ↑ | Anaerobic bacteria degrade sulfur-containing amino acids, producing volatile sulfur compounds (VSCs) responsible for malodor. |
| Taste Impairment | *Lactobacilli* | - | ↑ | Acidic metabolites disrupt sensory pathways, impairing taste perception. |
| Burning Mouth Syndrome | *Streptococcus spp.*, *Rothia spp.*, *Bergeyella spp.*, *Granulicatella spp.* | - | ↑ | Altered microbial communities influence inflammatory and sensory pathways, contributing to symptomatic manifestations. |
| Oral Thrush | *Candida parapsilosis*, *Candida krusei*, *Candida tropicalis* | *Candida albicans*, *C. glabrata*, *C. dubliniensis*, *C. guilliermondii* | ↑ | Fungal overgrowth occurs due to weakened immunity, poor hygiene, or comorbidities; mechanisms include adhesion, biofilm formation, hyphal development, and enzymatic degradation of host defenses. |
| Systemic Diseases | | | | |

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| IBD | - | *P. gingivalis*, *F. nucleatum* | ↑ | Oral bacteria translocate to the gut microbiome, compromising epithelial integrity and exacerbating dysbiosis. |
| Atherosclerosis | *Prevotella nigrescens*, *Parvimonas micra* | *S. mutans*, *P. gingivalis*, *P. endodontalis*, *T. denticola*, *T. forsythia*, *P. intermedia*, *A. actinomycetemcomitans*, *Eubacterium spp.*, *Campylobacter rectus* | ↑ | Dysbiosis-induced systemic inflammation, oxidative stress, and platelet aggregation contribute to cardiovascular risks. |
| Diabetes Mellitus | *Capnocytophaga* | *P. gingivalis*, *T. forsythia* | ↑ | Hyperglycemia promotes microbial imbalances and oxidative stress, intensifying inflammation. |
| Obesity | *Proteobacteria*, *Chloroflexi*, *Firmicutes* | - | ↑ | Migration of oral bacteria to the gut alters microbial composition and disrupts metabolic homeostasis. |
| Alzheimer's Disease | - | *P. gingivalis*, *T. forsythia*, *T. denticola* | ↑ | Neuroinflammation driven by oral microbiota products accelerates neurodegeneration and disease progression. |
| Parkinson's Disease | - | *P. gingivalis* | ↑ | Dissemination of *P. gingivalis* and its gingipains induces systemic inflammation, hypercoagulability, and exacerbation of neurodegeneration, linking oral health to PD pathology. |

| | | | | |
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| Rheumatoid Arthritis | *Prevotella spp.*, *Veillonella spp.*, *Lactobacillus salivarius* | *P. gingivalis*, *A. actinomycetemcomitans* | ↑ | Dysbiosis amplifies inflammatory processes, with *P. gingivalis* promoting protein citrullination and autoantibody production (ACPA), exacerbating RA symptoms. |
| Systemic Lupus Erythematosus | *Veillonella spp.*, *Streptococcus spp.*, *Prevotella spp.* | *T. forsythia*, *T. denticola* | ↑ | Oral dysbiosis and periodontal inflammation activate immune pathways, potentially exacerbating autoimmune responses in SLE. |
| Cancer | *Streptococcus oralis*, *S. mitis*, *S. sanguinis*, *Lactobacillus fermentum*, *L. acidophilus*, *Bifidobacterium adolescentis* | *P. gingivalis*, *F. nucleatum* | ↑ | Invasion by oncogenic pathogens and production of tumor-promoting agents, such as lipopolysaccharides, initiate and exacerbate carcinogenesis. |

## METHOD

A literature review was conducted on the impact of Gram-negative bacteria on oral health, focusing on terms such as Bacteria, Gram-negative bacteria, and Oral health, relevant studies were sourced from databases like PubMed, and SCOPUS, as well as search engines and institutional repositories.

## DISCUSSION

Oral health is a critical factor in assessing the health status of populations and serves as a key indicator of overall well-being (Okolo et al., 2024). The mouth hosts are the second most diverse microbial community in the human body, with over 700 bacterial species, disruptions in the balance of this oral ecosystem can lead to dysbiosis, allowing harmful bacteria to thrive and contribute to the development of conditions such as dental caries, gingivitis, and periodontitis (Hejran et al., 2024; Baker et al., 2024). Bacterial plaque, which adheres to surfaces, causes localized infections, and is resistant to antimicrobial treatments, plays a significant role in these diseases, caries and periodontitis are the most common oral diseases and are often linked to oral dysbiosis (Mitra, A. 2024).

Odontogenic infections can spread rapidly, potentially affecting neurovascular structures and compromising respiratory pathways, these infections are classified as simple or complex, with simple infections being localized and slower in progression, while complex infections can spread quickly, involving multiple tissues and upper airways (Soiniemi et al., 2024), these infections are usually polymicrobial, involving various facultative anaerobes such as: Campylobacter rectus: Associated with periodontal diseases, it triggers infections by promoting inflammation in the gums and damaging connective tissue, poor oral hygiene and plaque buildup facilitate its growth (Krishnamurthy et al., 2024). Veillonella spp: These bacteria thrive in dental biofilms and contribute to infections indirectly by metabolizing lactate produced by other bacteria, this creates an acidic environment, exacerbating gingivitis and caries (Ozturk et al., 2023; Bostanghadiri et al., 2024). Eikenella corrodens: Found in dental plaque and linked to periodontal infections, endodontic infections, and abscesses, it can invade soft tissues due to trauma or dental procedures, causing localized infections (Yuan et al., 2024). Capnocytophaga spp.: These bacteria are opportunistic pathogens that can lead to periodontal disease, particularly in immunocompromised individuals, they are also implicated in localized oral infections and systemic conditions if they enter the bloodstream (Nix et al., 2024).

Streptococcus anginosus is facultative anaerobic bacterium that is part of the normal oral flora but can become pathogenic under certain conditions, it is commonly associated with abscess formation in the oral cavity, as well as other infections such as endocarditis and soft tissue infections, known for its ability to cause purulent infections, it can sometimes be found in deeper tissues of the oral cavity, especially when there is an imbalance in the oral microbiome (Bloch et al., 2024). Streptococcus anginosus is a member of the Streptococcus milleri group and plays a role in both localized and systemic infections, particularly in immunocompromised individuals, and Streptococcus viridans group refers to a diverse collection of alpha-hemolytic, which are part of the normal microbiota of the mouth, throat, and respiratory tract, these bacteria are often involved in the formation of dental plaque and can contribute to the development of dental caries and periodontal diseases (Periferakis et al., 2024). Streptococcus viridans species, including Streptococcus mutans (a key cariogenic agent), are also implicated in infective endocarditis when they enter the bloodstream through oral procedures or poor oral hygiene (Senthil Kumar et al., 2024), the viridans group bacteria are characterized by their ability to produce a greenish discoloration (viridis) on blood agar due to partial hemolysis of red blood cells (Naorem et al., 2024). In addition to periodontal disease, dental caries and malocclusion are also highly prevalent worldwide, affecting both developed and developing nations. Around 65% of the population is affected by caries, with Streptococcus mutans identified as a primary cariogenic agent (Shehab et al., 2024). Dental abscesses, arising from untreated dental infections, are also common and can be very painful. While antibiotics are often considered for treatment, their use remains controversial due to the complexity of bacterial resistance (Wu et al., 2024).

Both Streptococcus anginosus and Streptococcus viridans are important members of the oral microbiome that, while typically harmless, can become pathogenic under certain circumstances, contributing to various oral and systemic infections, along with strict anaerobes like: Prevotella is a genus of gram-negative, obligate anaerobic bacteria found in the human oral cavity, as well as in the respiratory and gastrointestinal tracts,these bacteria are commonly involved in periodontal diseases, including gingivitis and periodontitis, and are associated with infections such as abscesses and soft tissue infections (George et al., 2024). Prevotella species are particularly important in the pathogenesis of chronic periodontitis, where they contribute to inflammation, tissue destruction, and bone loss, they

can also be implicated in other systemic infections, particularly in immunocompromised individuals, these species are known for their ability to produce various enzymes that break down proteins and other molecules, which can contribute to tissue destruction in the host (Williams et al., 2024; Uzunoğlu et al., 2024).

Fusobacterium is a genus of gram-negative, anaerobic bacteria that are common residents of the oral cavity and are involved in various oral and systemic infections, these bacteria play a significant role in the development of periodontal diseases, including periodontitis and abscesses, as well as in the progression of dental caries. Fusobacterium species are highly adhesive to host tissues, which allows them to contribute to biofilm formation on dental surfaces, where they interact with other pathogens to form complex microbial communities. Fusobacterium has also been implicated in systemic conditions such as colorectal cancer and cardiovascular diseases, as the bacteria can translocate to other parts of the body through the bloodstream (Deng et al., 2024). Bacteroides is a genus of gram-negative, obligate anaerobic bacteria that are part of the normal microbiota of the human mouth, intestines, and other mucosal surfaces. In the oral cavity, Bacteroides species are involved in periodontal diseases and are often found in subgingival plaque of individuals with periodontitis, they can contribute to tissue destruction by producing enzymes that degrade host tissues and by promoting inflammation, while generally considered part of the normal flora, Bacteroides species can become pathogenic under conditions of dysbiosis, leading to abscesses and infections in the oral cavity and other parts of the body, these bacteria are also known for their ability to resist various antimicrobial agents, which can complicate treatment of infections (Baima et al., 2024; Nalage et al., 2024). Peptostreptococcus, Prevotella, Fusobacterium, and Bacteroides are all key players in the oral microbiome, contributing to both normal oral health and, when the balance is disrupted, to the development of periodontal diseases, abscesses, and other infections, these bacteria are often involved in polymicrobial infections, where they interact with other pathogens to promote inflammation and tissue destruction, and in some cases, can lead to systemic health complications, these bacteria thrive in anaerobic environments like periodontal abscesses, contributing to tissue damage and disease progression.

Efforts to promote oral health are essential and include public health programs aimed at improving oral hygiene and habits, particularly within primary healthcare settings, these programs target risk factors, offer specialized care, and seek to achieve comprehensive coverage across different population groups (Ojeyinka et al., 2024). Research on oral diseases has expanded, particularly on how these conditions relate to systemic health. Periodontal disease, affecting about 11.8% of the general population, is the most severe form of oral disease and a leading cause of tooth loss, it is primarily caused by bacterial dysbiosis and contributes to systemic inflammation, linking it to cardiovascular diseases, diabetes, respiratory issues, and rheumatoid arthritis (Nagari et al., 2024). The biological mechanisms connecting periodontal disease to systemic conditions include bacteremia, endotoxemia, and low-grade inflammation (Sarwari et al., 2024). Dysbiotic bacteria and their byproducts can enter the bloodstream, leading to distant infections or exacerbating systemic inflammation. Periodontal disease starts with gingivitis, an inflammation of the gums, and can progress to periodontitis as irritants like calculus and bacterial plaque cause bone loss around the teeth (Qilichovna, A. M. 2024).

Gram-negative bacteria play a significant role in the progression of oral diseases, particularly due to their ability to develop antimicrobial resistance (Mei et al., 2024). One of the key mechanisms for

resistance is biofilm formation, where bacteria cluster together in a protective matrix, making them harder to treat with antibiotics. Biofilms are responsible for over 65% of all microbial infections, with several mechanisms contributing to their resistance, such as the inactivation of antibiotics, nutrient limitations, and the persistence of resistant bacterial cells (Zafer et al., 2024), for managing bacterial infections in oral diseases, particularly those caused by resistant strains, chlorhexidine is commonly used. This broad-spectrum antiseptic is effective as a topical treatment for gingivitis and in protocols to prevent the spread of infections through the bloodstream. In count, dietary modifications play a significant role in controlling caries formation, with foods rich in fatty acids, proteins, and polyphenols offering protective benefits. Ozonated vegetable oils, which exhibit antimicrobial and regenerative properties, have shown promise in combating gram-positive bacteria, though their efficacy against gram-negative bacteria remains under investigation, with some promising results Table 2 (Khan et al., 2024).

***Table 2*** *(Summarizing Key Aspects of Oral Health, Microbial Community, Common Oral Diseases, and Their Connection to Systemic Health)*

| | |
|---|---|
| Oral Health and General Well-being | Oral health is a critical indicator of overall health, affecting psychological, emotional, and physical well-being, poor oral health is linked to diseases like dental caries, gingivitis, and periodontitis. |
| Oral Microbial Community | The mouth contains over 700 bacterial species, forming the second most diverse microbial community in the human body. Dysbiosis (microbial imbalance) can lead to infections and oral diseases. |
| Common Oral Diseases | - **Dental Caries**: Caused by microbial imbalance, particularly from *Streptococcus mutans*.<br>- **Gingivitis**: Inflammation of gums.<br>- ***Periodontitis***: Inflammation that cause's tissue and bone loss. |
| Role of Bacterial Plaque | Plaque is a biofilm that adheres to surfaces in the mouth, causing infections and being resistant to antimicrobial treatments. It's involved in the progression of caries and periodontal diseases |
| Key Pathogenic Bacteria | Infections originating from the teeth can spread to surrounding tissues, including neurovascular structures and respiratory pathways. These can be classified as simple (localized) or complex (rapid, polymicrobial infections). |
| Anaerobic Bacteria Involved in Infections | - ***Prevotella***: Associated with periodontal diseases, gingivitis, and systemic infections. Known for enzyme production that leads to tissue destruction. |

| | |
|---|---|
| | - ***Fusobacterium***: Involved in periodontitis and abscesses; linked to systemic diseases like cardiovascular disease.<br>- ***Bacteroides***: Found in periodontal plaque, contributes to tissue destruction and inflammation. |
| Infectious Interactions | These bacteria often interact in polymicrobial infections, contributing to tissue damage, inflammation, and sometimes systemic complications like sepsis. |
| Public Health Programs | Programs aimed at improving oral hygiene, targeting risk factors, and providing specialized care to reduce the incidence of oral diseases and their systemic effects |
| Prevalence of Oral Diseases | - **Periodontal Disease**: Affects 11.8% of the population, leading to tooth loss and contributing to systemic conditions.<br>- **Dental Caries**: Affects 65% of the population, with Streptococcus mutans as the main contributor. |
| Biological Mechanisms | Periodontal disease can lead to bacteremia, endotoxemia, and low-grade inflammation. Dysbiotic bacteria can enter the bloodstream, exacerbating systemic inflammation and distant infections |
| Pathogenesis of Periodontal Disease | Begins with gingivitis, progressing to periodontitis, causing bone loss and inflammation. Linked to systemic diseases like cardiovascular disease, diabetes, and rheumatoid arthritis |
| Malocclusion and Dental Abscesses | Malocclusion and dental abscesses are common worldwide and can cause significant pain. Abscesses arise from untreated infections. Antibiotic use is controversial due to bacterial resistance |

| | |
|---|---|
| Role of Gram-Negative Bacteria | Gram-negative bacteria (*Fusobacterium, Bacteroides*) contribute to oral diseases and are resistant to antibiotics due to biofilm formation. Biofilms make infections harder to treat, accounting for over 65% of microbial infections. |
| Antibiotic Resistance | Gram-negative bacteria exhibit resistance through biofilm formation, nutrient limitation, and antibiotic inactivation, these bacteria are harder to treat with conventional antimicrobial agents. |
| Treatment of Oral Infections | - **Chlorhexidine**: Used topically for gingivitis and to prevent the spread of infections through the bloodstream.<br>- **Ozonated Vegetable Oils**: Show antimicrobial effects against gram-positive bacteria, with limited results against gram-negative bacteria. |
| Dietary Modifications | Foods rich in fatty acids, proteins, and polyphenols can help protect against caries formation. |

**MYCOPLASMA**

Mycoplasma is a genus of bacteria characterized by the absence of a cell wall, making them distinct from most other bacteria, these organisms are small, pleomorphic (able to change shape), and generally do not have a defined shape, which allows them to appear as spherical or filamentous structures. Mycoplasma species are known to be facultative or obligate anaerobes, depending on the species (Vastel et al., 2024). Because they lack a cell wall, they are resistant to many common antibiotics that target cell wall synthesis, such as penicillin. Mycoplasma infections are challenging to diagnose because these bacteria lack typical cell wall structures and often grow slowly in cultures (Chen et al., 2024). Consequently, PCR (Polymerase Chain Reaction) and other advanced molecular techniques are commonly used for detection and identification of Mycoplasma species.

One of the most well-known species in this genus is Mycoplasma pneumoniae, which causes respiratory infections, primarily pneumonia (Wei et al., 2024). However, several other Mycoplasma species are part of the normal microbiota in humans, including those that inhabit the oral cavity, genitourinary tract, and respiratory tract. In the oral cavity Mycoplasma species, such as Mycoplasma fermentans and Mycoplasma salivarium, have been identified, though they are typically considered opportunistic pathogens, their role in oral diseases is not fully understood, but they may contribute to conditions such

as periodontitis and other chronic infections due to their ability to adhere to mucosal surfaces and evade immune responses (Leonovich, O. A. 2024).

Moreover; this investigation revealed that Mycoplasmas, Gram-negative bacteria, and certain Gram-positive bacteria possess a common protein antigen with a molecular weight ranging between 42,000 and 48,000. This protein antigen was detected in all Mycoplasmas, Acholeplasma laidlawii, and Gram-negative bacteria examined, as well as in Staphylococcus aureus. The cross-reactive antigen, identified as the 45,000 molecular weight (45K) protein, was present in all Mycoplasmas, the tested Gram-negative bacteria, and Staphylococcus aureus, a Gram-positive bacterium. The precise function and cellular localization of the 45K protein within these organisms remain undetermined. The 45K protein, which is a significant constituent of Mycoplasmas, is present in both the cytoplasmic and membrane fractions of the cells. However, it is not exposed on the surface of these microorganisms. Monoclonal antibodies (MAbs) have been shown to recognize the epitopes of the 45K protein in Mycoplasmas, with varying blotting patterns depending on the species. The N-terminal amino acid sequence of the purified 45K protein from A. laidlawii, M. fermentans, M. hyorhinis, E. coli, and S. aureus, along with its functional role in these microorganisms, is currently under investigation (Sasaki, 1991; Gaurivaud & Tardy, 2022).

## SYSTEMIC CONDITIONS LINKED TO ORAL HEALTH

Oral health is essential for overall well-being, as poor oral hygiene and untreated dental diseases can contribute to a range of systemic health conditions. For example, gum disease is linked to an increased risk of cardiovascular diseases, as oral bacteria can enter the bloodstream and cause inflammation in blood vessels, poor oral health also complicates diabetes management, while uncontrolled diabetes exacerbates gum disease (fouad Merza et al., 2024). Oral infections can lead to respiratory issues, such as pneumonia, when bacteria are aspirated into the lungs, also gum disease has been associated with pregnancy complications, including premature birth and low birth weight, and may increase the risk of Alzheimer's disease (Ouyang et al., 2024). Chronic oral infections can worsen kidney disease, and individuals with osteoporosis are at a higher risk for tooth loss due to jawbone deterioration (Chan, W. S. H. 2024; Cherry-Peppers et al., 2024). Poor oral health is linked to an increased risk of certain cancers, such as pancreatic and head and neck cancers, likely due to the chronic inflammation caused by oral infections (Aghili et al., 2024).

Good oral health offers numerous benefits beyond dental care, improving social, psychological, and physical health, regular dental care not only prevents periodontal disease but also helps identify patients at higher risk for serious systemic conditions (Tiwari, T., and Randall, C. L. 2024), routine dental visits can reduce overall healthcare costs, as individuals with good oral hygiene tend to require fewer medical interventions (Mishu et al., 2024). Systemic conditions influenced by oral health include atherosclerosis, pulmonary disease, diabetes, osteoporosis, kidney disease, and pregnancy complications (Chatzopoulos et al., 2024). Thus, maintaining good oral hygiene is critical for both dental and overall health, and stronger collaboration between dental and medical professionals is essential to address the wide-reaching health impacts of oral diseases.

Additionally; the oral cavity serves as a reflection of systemic health, with numerous systemic conditions manifesting as oral symptoms. Conversely, oral pathologies can profoundly influence systemic health, compromising nutritional intake, overall well-being, and quality of life, while

exacerbating stress and anxiety levels. Affecting approximately 3.5 billion individuals globally, oral diseases, including oral and lip cancers, rank among the 15 most prevalent oral health conditions. The World Health Organization (WHO) underscores the significance of oral health as a critical determinant of overall health, well-being, and life quality. Addressing periodontitis necessitates a multifaceted, interdisciplinary approach that integrates personalized medicine and holistic care paradigms. The oral microbiome plays an integral role in the etiology of various systemic and oral pathologies, potentially acting as a cornerstone in the intricate relationship between oral and systemic health. In 2017, the World Workshop on Oral Medicine emphasized the "oral microbiome" as a pivotal area of research, particularly in understanding the pathogenesis of oral mucosal diseases, including potentially malignant conditions and oral cancers. Studies have demonstrated differences in the composition and function of the oral microbial communities in oral cancer patients, with or without lymph node metastases, suggesting its potential prognostic value. Oral dysbiosis contributes significantly to periodontitis, driving a personalized disease trajectory shaped by individual microbiome disturbances and host-specific risk factors. Periodontitis disrupts the equilibrium of pro-inflammatory and anti-inflammatory genetic responses, while cancer therapies can further damage dental tissues and disturb the oral microbiome. Emerging therapeutic strategies aimed at restoring microbiome balance and mitigating dysbiosis hold promise for preventing disease progression and minimizing therapy-related complications. Oral health is increasingly recognized as a cornerstone of overall well-being, with oral disorders substantially impacting functional, social, and psychological dimensions. Preventative measures are essential for managing oral diseases and advancing the integration of personalized, multidisciplinary, and holistic medical approaches (Varoni & Rimondini, 2022; Sabbah et al., 2019).

## IMPACT OF MEDICINAL PLANTS ON ORAL HYGIENE

Plants have been widely used in traditional and modern medicine to support oral health due to their rich bioactive compounds, these natural substances offer antimicrobial, anti-inflammatory, antioxidant, and wound-healing properties, which play a significant role in maintaining oral hygiene, treating infections, and promoting the overall health of the oral cavity (Alimyar et al., 2023; Niazi, P., and Monib, A. W. 2024). Here's a detailed explanation of the role of various plants and how they can be used for oral care:

### A. Antimicrobial Activity

Certain plants are highly effective at reducing harmful oral bacteria, fungi, and viruses. Neem (Azadirachta indica) is renowned for its antibacterial properties, making it a popular ingredient in herbal toothpaste and mouth rinses. Using neem twigs as natural toothbrushes or gargling with neem-infused water can significantly reduce plaque buildup and combat bacteria such as Streptococcus mutans, a primary cause of cavities. Similarly, tea tree oil, derived from Melaleuca alternifolia, has potent antimicrobial effects that help manage oral infections. A few drops of diluted tea tree oil in warm water can be used as a mouthwash to fight bacteria. Clove (Syzygium aromaticum) is another plant with strong antimicrobial properties due to its eugenol content, chewing on cloves or using clove oil (diluted in a carrier oil) as a topical application can relieve tooth pain and prevent bacterial growth Figure 1 (de Medeiros Silva et al., 2024; Mansoor et al., 2024; Silva et al., 2024).

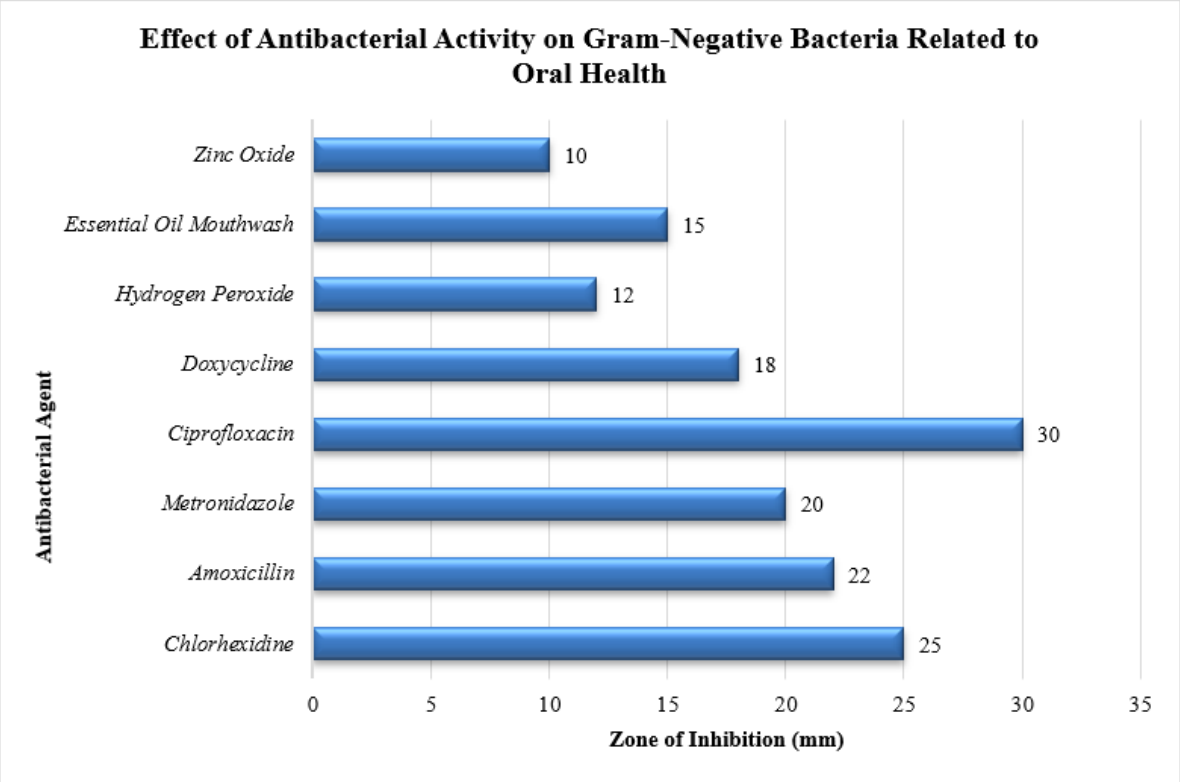


***Figure 1*** *(Illustrates the antibacterial activity of various agents against Gram-negative bacteria associated with oral health, measured by the zone of inhibition in millimeters. Ciprofloxacin demonstrates the highest efficacy, with a 30 mm zone of inhibition, indicating strong antibacterial activity against Aggregatibacter actinomycetemcomitans. Chlorhexidine and Amoxicillin also exhibit significant effects, with zones of 25 mm and 22 mm, respectively, particularly effective against Porphyromonas gingivalis and Fusobacterium nucleatum. Conversely, agents like Zinc Oxide and Hydrogen Peroxide show comparatively low efficacy, with inhibition zones of 10 mm and 12 mm, respectively. These results underscore the variability in antibacterial effectiveness, highlighting the need for targeted selection of agents to manage oral health conditions caused by Gram-negative pathogens.)*

## B. Anti-inflammatory Effects

Chronic gum inflammation is a common problem, and plants with anti-inflammatory properties can offer relief. Aloe vera gel is well-known for its soothing properties. Applying fresh aloe vera gel to inflamed gums or using aloe vera-based toothpaste can reduce redness and swelling. Chamomile (Matricaria chamomilla), often used as a tea, has anti-inflammatory effects that can soothe oral tissues. Rinsing your mouth with cooled chamomile tea or applying a chamomile compress to irritated areas helps manage gum inflammation and can be especially soothing for oral ulcers (Sediqi et al., 2023).

## C. Antioxidant Properties

Oxidative stress plays a significant role in the progression of periodontal disease, and antioxidant-rich plants help neutralize free radicals, green tea (Camellia sinensis) is particularly effective due to its catechins, which offer both antimicrobial and antioxidant benefits, drinking unsweetened green tea or using it as a mouth rinse helps reduce plaque formation, combat gum inflammation, and promote

healthier gums. Its catechins inhibit the growth of bacteria associated with dental plaque and reduce bad breath as well (Fahmi et al., 2024).

### D. Promotion of Healing

Plants with wound-healing properties are invaluable for oral tissue repair, particularly after dental procedures or injuries. Calendula (Calendula officinalis) is a well-known healing herb. A calendula mouth rinse, made by steeping dried calendula flowers in boiling water, can be used to soothe oral sores, speed up tissue repair, and reduce inflammation. Licorice root (Glycyrrhiza glabra) is another excellent option for promoting oral health, chewing on dried licorice root or using licorice root extract in oral care products can protect against oral bacteria while aiding in the healing of damaged tissues (Baseer et al., 2024; Salama et al., 2024; Gohil et al., 2024).

### E. Reduction of Halitosis (Bad Breath)

Bad breath is often caused by volatile sulfur compounds (VSCs) produced by bacteria in the mouth. Certain plants neutralize these compounds and leave the mouth feeling fresh. Parsley (Petroselinum crispum) contains chlorophyll, which acts as a natural deodorizer, chewing fresh parsley leaves after meals can help neutralize odors (Awulachew, M. T. 2024). Mint (Mentha spp.) is another popular choice for combating halitosis, the menthol in mint inhibits odor-causing bacteria, and mint leaves can be chewed directly or steeped in water to create a refreshing mouthwash (Ramabrahmareddy, D. 2024).

### F. Plaque and Tartar Control

Preventing plaque buildup is essential for maintaining healthy teeth and gums. Cranberries (Vaccinium macrocarpon) contain proanthocyanidins, which prevent bacteria from adhering to the surfaces of teeth. Consuming unsweetened cranberry juice or using cranberry extract in oral care products can reduce the risk of cavities and gum disease. Miswak (Salvadora persica), a traditional chewing stick, has been used for centuries for its natural plaque-fighting properties. It contains fluoride, tannins, and saponins, which strengthen teeth and fight bacteria, using a miswak stick as an alternative to a toothbrush can be highly effective in maintaining oral hygiene (Abdellatif et al., 2024; Asim et al., 2024).

## RECOMMENDATIONS

A. Enhanced Public Awareness: Conduct educational campaigns to highlight the connection between oral health and systemic health, particularly the role of Gram-negative bacteria like Porphyromonas gingivalis. Emphasize the importance of oral hygiene in reducing the risk of systemic conditions such as cardiovascular diseases, diabetes, and adverse pregnancy outcomes.
B. Improved Diagnostic Methods: Develop and promote advanced diagnostic tools to identify the presence and activity of Gram-negative bacteria in the oral cavity, focusing on early detection of high-risk pathogens like P. gingivalis. Encourage regular dental check-ups that include assessments of the oral microbiome balance.
C. Targeted Treatment Strategies: Promote the use of antimicrobial therapies tailored to combat Gram-negative bacteria while preserving the balance of beneficial oral microbiota. Explore and implement treatment modalities addressing biofilm resilience, such as enzymatic biofilm disruptors or combination therapies.

D. Preventive Measures: Advocate for daily oral hygiene practices, including proper brushing, flossing, and the use of antimicrobial mouth rinses. Support dietary guidelines that reduce the growth of harmful bacteria, such as limiting sugar intake and encouraging probiotic-rich foods.
E. Research and Development: Fund and prioritize research on the mechanisms of virulence and resistance in Gram-negative bacteria, particularly their ability to form biofilms and evade immune responses. Investigate novel approaches to manage chronic inflammation caused by these pathogens and mitigate systemic effects.
F. Interdisciplinary Collaboration: Foster collaboration between dentists, physicians, and microbiologists to develop integrated treatment plans that address both oral and systemic health. Train healthcare professionals to recognize and manage the oral-systemic health connection effectively.
G. Community-Level Initiatives: Implement community oral health programs, especially in underserved areas, to provide access to preventive care and education about Gram-negative bacteria's impact on health. Encourage the development of policies that integrate oral health into overall healthcare frameworks.
H. Use of Plants in Oral Care: Toothpaste and Mouthwash: Look for products that include extracts of neem, aloe vera, green tea, or licorice root. Alternatively, make your own by adding essential oils (like tea tree or clove oil) to baking soda or coconut oil. Teas and Rinses: Prepare herbal teas from chamomile, green tea, or calendula, let them cool, and use them as mouth rinses to reduce inflammation and kill bacteria. Chewing Sticks and Leaves: Use miswak sticks or chew fresh leaves of parsley and mint for their deodorizing and antimicrobial effects. Topical Applications: Apply aloe vera gel or diluted clove oil directly to inflamed or painful areas in the mouth for soothing relief. Dietary Inclusion: Incorporate antioxidant-rich foods like cranberries and green tea into your diet for ongoing oral health benefits.

## CONCLUSIONS

Gram-negative bacteria play a significant role in the development of oral diseases like caries, gingivitis, and periodontitis, these bacteria contribute to treatment resistance, complicating management and increasing the risk of systemic complications, many patients may not realize the link between oral health and conditions like heart or bone diseases, but addressing oral issues can prevent serious health problems, the oral microbiome is highly diverse, with over 700 species, and its unique structure supports microbial communities essential for both oral and overall health, these interactions are key to improving both oral and systemic health outcomes. Each plant contributes uniquely to oral health, from reducing bacteria and inflammation to promoting healing and freshening breath. Neem, clove, tea tree oil, green tea, and miswak stand out as particularly versatile and widely applicable plants for oral hygiene. Choose plants based on specific oral health needs and incorporate them into your oral care routine accordingly.

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