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Periodontal disease as a chronic systemic burden: physiological insights, market trends, and therapeutic landscape

Abstract

Periodontal disease is a common, progressive inflammatory condition with complex causes and significant implications for both oral and overall health. This paper begins by reviewing the physiology of healthy periodontal tissues, followed by an explanation of the pathogenesis and progression of periodontal disease. In addition to its localized effects, periodontitis is increasingly recognized for its strong epidemiological associations with a range of systemic illnesses, including cardiometabolic disorders, neurodegenerative diseases, autoimmune conditions, respiratory infections, and cancer. North America currently dominates the periodontal therapeutics market, while the Asia Pacific region is rapidly establishing itself as the fastest-growing market. The global market for periodontal therapeutics continues to expand, driven by rising disease prevalence, greater awareness of oral health, an aging population, and technological advancements. Existing products such as ARESTIN, ATRIDOX, Emdogain, and BioMend membranes enhance treatment outcomes through targeted drug delivery, guided tissue regeneration, and improved surgical healing. This paper also discusses promising innovations currently in clinical trials, including advanced dentifrices, novel antibiotics, and stem cell therapies, which highlight the potential for transformative shifts in periodontal care. Together, these findings and innovations reflect a dynamic and rapidly evolving market focused on not only halting disease progression but also restoring periodontal health through scalable, personalized, and regenerative therapies.

Keywords: periodontal disease, gum disease, periodontitis, gingivitis, oral health, systemic disease associations

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Abbreviations: LPS, lipopolysaccharide; AD, alzheimer's disease; PD, parkinson's disease; BBB, blood-brain barrier; RA, rheumatoid arthritis; PAD, peptidyl arginine deiminase enzyme; ACPAs, anti-citrullinated protein antibodies; TLR, toll-like receptor; COPD, chronic obstructive pulmonary disease; CAGR, compound annual growth rate; WHO, World Health Organization; NIH, national institutes of health; MMP-8, metalloproteinase-8; MPDI, multidisciplinary digital publishing institute; GTR, guided tissue regeneration; GBR, guided bone regeneration; EDTA, ethylene diamine tetra acetic acid

Introduction

Periodontal disease, commonly referred to as gum disease, is a chronic inflammatory condition that progressively damages the supporting structures of the teeth.[1,2] Gum disease progresses from gingivitis, a reversible inflammation of the gums, to periodontitis, where bacteria damage the supporting bone and tissues.[3,4] If left untreated, it can lead to gum recession, infection, tooth mobility, and ultimately tooth loss.

Despite being largely preventable, periodontal disease continues to be a prevalent global health issue, affecting over one billion people annually.[3] Severe periodontitis affects over 10% of the global adult population, ranking it as the 11th most common disease worldwide and surpassing even cardiovascular disease in prevalence. Beyond its oral effects, periodontal disease is also epidemiologically linked to various chronic conditions, underscoring its significance as a global systemic health concern.[5]

This paper begins by outlining the physiological characteristics of healthy gums and the physiological changes that occur during the onset and progression of periodontal disease. It then provides an in-depth review of epidemiological associations between periodontal disease and systemic illnesses, followed by a comprehensive analysis of market trends, current therapeutic approaches, and emerging innovations anticipated to transform the future of periodontal care.

Anatomy and physiology of healthy gums

The gums are soft tissues in the upper and lower jaws that surround the base of the teeth. Their primary function is to hold the teeth in place, protect them from external damage, and cover the underlying jawbone that supports the teeth, helping to maintain overall oral stability and health.[6]

The gums consist of multiple soft tissue layers that support and protect the roots of the teeth. The maxillary and mandibular labial frena are thin bands of tissue connecting the inside of the lips to the upper and lower gums at the front of the mouth, respectively.[3] The alveolar mucosa is a bright red mucous membrane that lines the inside of the cheeks, lips, and floor of the mouth. The marginal gingiva is a narrow band of tissue that surrounds the base of the teeth and is not directly attached to them, allowing it to be gently moved during dental examinations. In contrast, the attached gingiva is firmly bound to the underlying bone and cannot be shifted.[6] The interdental gingiva, or papilla, fills the space between adjacent teeth, playing an important role in protecting the underlying structures.

Healthy gums are typically firm and fit tightly around the teeth, forming a protective seal.[4,6] The color of healthy gums can range from light pink to dark pink or brown, depending on an individual's natural pigmentation.[7]

Overview of periodontal disease

Disease pathogenesis and progression

Periodontal disease, or gum disease, is a condition involving inflammation and infection of the tissues that support and anchor the teeth.[4,6] The disease frequently progresses asymptomatically, with clinical signs often remaining undetected until the advanced stages of the condition.[8] Gum disease progresses through four stages, beginning with gingivitis, where red, swollen gums may bleed during brushing or flossing. At this early stage, there is no bone loss, and the condition is reversible with proper care. If left untreated, it advances to mild periodontitis, where bacteria invade below the gumline, forming pockets that trap plaque and are difficult to clean. Moderate periodontitis follows, marked by damage to the ligaments and bone supporting the teeth, often accompanied by bad breath, pus, and discomfort. In the final stage of advanced periodontitis, ongoing bone loss can cause teeth to loosen and eventually fall out.[4]

Primary causes and factors

The most common cause of gum inflammation is plaque, a nearly invisible, bacteria-rich film that builds up where the teeth and gums meet.[9] If not removed daily, dental plaque can harden into tartar, or calculus.[10,11] Unlike plaque, tartar can only be removed through professional cleaning by a dentist or dental hygienist. As bacteria in plaque and tartar feed on sugars in the mouth, they release substances that irritate and inflame the gums. These conditions are more likely to occur in smokers, individuals with metabolic conditions like diabetes, pregnant women due to hormonal changes, and those genetically predisposed to gum disease. Additionally, certain medications, such as immunosuppressants or drugs for cardiovascular conditions, can enlarge the gums, making proper cleaning more difficult and increasing the risk of infection.[9]

Diagnosis and prevention strategies

Periodontal disease is diagnosed using several methods that assess the health of the supporting structures around the teeth. Key clinical measures include pocket depth and clinical attachment loss. Both are evaluated using manual periodontal probes, though variations in technique can affect accuracy. Healthy pockets are typically 1 to 3 millimeters deep, while deeper ones may indicate disease. Bleeding on probing is another indicator of periodontal disease. Tooth mobility, assessed manually using the Miller index, provides insight into structural integrity. Imaging also plays a vital role in periodontal disease prognosis. 2D radiography, such as panoramic and intraoral X-rays, is commonly used to evaluate alveolar bone loss, but it lacks detail on soft tissue conditions. 3D imaging, such as CT scans, offers more precise bone visualization but is limited by high costs and radiation exposure. MRI, while effective for soft tissue imaging, remains impractical for dental applications due to poor visibility of hard tissues. Additionally, reviewing the patient's medical history helps identify risk factors, such as smoking or diabetes that may contribute to periodontal disease. Moreover, a dental professional may refer a patient to a periodontist, a specialist in diagnosing and treating gum disease, who can offer advanced treatment options beyond those typically available through a general dentist.[2,10]

Gum disease is not curable, but it can be effectively managed with proper treatment. While the structural support lost around the teeth usually cannot be fully restored, periodontal therapy can reduce infection and, in some cases, partially regenerate bone and tissue. Genetics also plays a role, as some individuals are more prone to the types of oral bacteria that cause gum disease. However, the earliest stage, gingivitis, is completely reversible if caught early through professional cleanings and consistent oral hygiene. To lower your risk of developing gum disease, maintain good oral hygiene by brushing your teeth two times daily, flossing once a day, and using an antibacterial mouthwash. Additionally, avoid smoking or using tobacco products, and visit your dentist regularly for cleanings and checkups.[4,12]

Epidemiological associations with systemic diseases

Periodontal disease constitutes a significant global health concern due to its established epidemiological associations with a range of chronic illnesses, including cardiometabolic disorders, neurodegenerative diseases, autoimmune disorders, respiratory infections, and certain cancers.[13,14]

Cardiometabolic disorders

Periodontitis is bidirectionally linked with cardiometabolic disorders, partly due to endotoxemia caused by bacterial lipopolysaccharide (LPS) entering the bloodstream. While the intestinal microbiota is the primary source of endotoxemia, dysbiotic periodontal bacteria may also contribute. Endotoxemia disrupts lipid metabolism by increasing harmful lipids and lowering protective cholesterol, promoting conditions such as cardiovascular disease, obesity, diabetes, and metabolic syndrome. Thus, endotoxemia serves as a key mechanistic connection between periodontal disease and cardiometabolic disorders.[15]

Neurodegenerative diseases

Periodontal disease has been increasingly implicated in the pathogenesis of neurodegenerative diseases, particularly Alzheimer's disease (AD) and, to a lesser extent, Parkinson's disease (PD). Several biological mechanisms have been proposed to explain the connection between periodontitis and neurodegenerative diseases, with most being centered around the systemic effects of chronic oral inflammation and the role of pathogenic bacteria.

One of the primary pathways involves systemic inflammation. Periodontitis induces the persistent release of pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α into the bloodstream. These cytokines can cross the blood-brain barrier (BBB) and contribute to neuroinflammation, a key process in the development and progression of AD and other neurodegenerative disorders.[16]

Another widely supported mechanism is the direct bacterial invasion of microbial components.[17,18] Pathogens commonly found in gingival and periodontal infections, specifically *Porphyromonas gingivalis*, may access the brain either hematogenously or via peripheral nerves. These bacteria and their virulence factors, such as gigipains, have been detected in AD patients and have been shown to contribute to hallmark features of the disease, including amyloid-β accumulation and tau phosphorylation.

Additionally, microbiome dysbiosis and vascular dysfunction associated with periodontitis may disrupt immune regulation and compromise the integrity of the BBB, facilitating entry of peripheral inflammatory mediators and pathogens into brain tissue.[19] Together, these mechanisms suggest that periodontitis may not only be a marker but also a potential contributor to neurodegenerative disease risk and severity.[16,19]

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Autoimmune and inflammatory disorders

There has been increasing evidence implicating that periodontitis is a contributor to autoimmune conditions, notably rheumatoid arthritis (RA), through several interconnected immunological and inflammatory mechanisms.

A central link is the activity of *Porphyromonas gingivalis*, a periodontal pathogen that expresses a unique peptidylarginine deiminase enzyme (PAD) capable of citrullinating host proteins. These altered proteins can trigger the production of anti-citrullinated protein antibodies (ACPAs), which are a defining feature of RA pathogenesis.[20]

Additionally, chronic periodontal inflammation elevates systemic levels of inflammatory cytokines such as TNF-α, IL-1β, and IL-6, which can intensify synovial inflammation and bone resorption in RA patients.[21,22] Toll-like receptor (TLR)-mediated immune activation by oral pathogens further drives autoimmune susceptibility by disrupting immune tolerance.

Epidemiological studies support this biological link, with individuals with periodontitis exhibiting a significantly increased risk of developing RA. This suggests that periodontal disease may not only share pathogenic pathways with RA but could also contribute to its onset and progression, making oral health an important consideration in autoimmune disease prevention and management.[23]

Respiratory infections and pulmonary disease

Respiratory conditions, including chronic obstructive pulmonary disease (COPD) and pneumonia, have shown growing associations with periodontitis in recent research.[24] After adjusting for common confounders such as smoking, individuals with periodontal disease have been shown to have a twofold increase in developing COPD.[13] A key mechanism is the aspiration of periodontal pathogens, such as *Porphyromonas gingivalis*, into the lower respiratory tract, where they may contribute to infection or inflammation, especially in elderly or hospitalized individuals.

In addition, systematic inflammation originating from periodontal tissues may exacerbate pulmonary disease. Elevated cytokines can contribute to airway inflammation and declining lung function.[25] Periodontal pathogens can also release enzymes that modify the respiratory epithelium, facilitating colonization by other pathogens.[24] Epidemiological studies support this connection, demonstrating that periodontitis can worsen the progression of COPD and increase the risk of respiratory diseases such as pneumonia, bronchitis, and emphysema. These findings suggest a bidirectional relationship between periodontal disease and respiratory conditions, highlighting the need to integrate oral care into respiratory and pulmonary disease prevention strategies.[26]

Periodontal disease and overall cancer risk

Recent studies have identified a 14% to 24% increase in overall cancer risk among individuals with periodontal disease. This association is biologically plausible and supported by several mechanistic pathways, including chronic systemic inflammation and microbial dysbiosis.[27]

Periodontitis drives persistent systemic inflammation characterized by elevated levels of pro-inflammatory cytokines.[28] These cytokines can promote tumorigenesis by inducing cell migration, enhancing cell proliferation, inhibiting apoptosis, and promoting angiogenesis, all of which are hallmarks of cancer development. Chronic systemic inflammation induces cellular stress through the generation of reactive oxygen and nitrogen species, which can cause DNA damage and promote genomic instability.[27]

Beyond inflammation, oral bacteria can contribute to cancer development via systemic effects following their entry into the bloodstream. Frequent bacteremia caused by periodontal pathogens can trigger widespread immune activation. *Porphyromonas gingivalis* has been shown to disrupt gut microbiota, elevate endotoxin levels, promote systemic inflammation, and evade immune detection via TLR-4 signaling. These effects contribute to oral and intestinal dysbiosis and are implicated in colorectal cancer.[27] *P. gingivalis* has been detected in colorectal tumors, and laboratory studies show its potential to transform colonic cells.[29] Other oral microbes, such as *Fusobacterium nucleatum*, *Gemella*, and *Peptostreptococcus*, are also strongly linked to colorectal cancer.[30]

Market landscape: size, trends, and segmentation

Global market size by region

The global periodontal therapeutics market was valued at $872.8 million in 2023 and is projected to grow at a compound annual growth rate (CAGR) of 7.2% from 2024 to 2030, reaching an impressive $3.53 billion by 2030. This growth is largely driven by the rising prevalence of periodontal diseases. According to a World Health Organization (WHO) report published in March 2023, severe periodontal conditions affect around 19% of the global adult population, accounting for over 1 billion cases. These include common but serious conditions such as gingivitis and periodontitis, which continue to pose major public health challenges. North America currently holds the largest share of the periodontal therapeutics market, while the Asia Pacific region is rapidly becoming the fastest-growing market, with other regions also experiencing notable growth, as illustrated in Figure 1.[31,32]

Figure 1 Illustration showing how teeth are anchored within the gums.

The image shows the how the teeth are anchored within the gums, with the teeth and surrounding tissues labeled.

The image shows the global periodontal therapeutics market segmented by distribution channel in 2023.

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North America

In 2023, North America held a 37.7% share of the periodontal therapeutics market, largely driven by the high prevalence of periodontal disease and supportive government initiatives. In the U.S. alone, around 42% of adults are affected by this condition, and the U.S. periodontal therapeutics market is expected to grow by a CAGR of 6.7% by 2030. Market growth in North America is further supported by active research and development efforts. For example, in August 2021, the University of Pennsylvania and the ADA Science & Research Institute received a $2 million National Institutes of Health (NIH) grant to study the oral mucosa, focusing on how the mouth's protective barrier responds to gum disease. Moreover, North America's widespread use of advanced diagnostic and treatment technologies, along with a large number of dental clinics and specialized care centers, reinforces its position as a leading market. Therefore, continued market growth in North America is expected due to high healthcare expenditure and a mature dental care infrastructure.[31,33]

Asia Pacific

The Asia Pacific periodontal therapeutics market is expected to reach $0.85 billion by 2030, growing at a CAGR of 6.9%. The region is expected to exhibit strong growth potential, fueled by a sizable target population, significant unmet clinical needs, and a developing healthcare infrastructure. The main driving factors are a rising population, particularly in countries like India and China, and lifestyle and dietary changes that contribute to an increase in periodontal disease diagnoses. Enhanced access to dental care and supportive government initiatives promoting oral health are also expected to boost market demand across the region.[31,32]

Latin America

The Latin American market is also projected to expand rapidly, largely due to a growing population and rising urbanization. This urban shift often brings lifestyle changes, including altered diets, greater tobacco consumption, and elevated stress, that contribute to the increasing prevalence of periodontal diseases across the region.[31]

Europe

Similarly, Europe is considered a promising market for periodontal therapeutics due to its large and aging population. The growing need for treatment among this demographic, combined with the region's robust healthcare infrastructure and well-developed dental care services, is driving demand for periodontal therapies.[31]

Middle East and Africa

The Middle East and Africa region is also considered a lucrative market within the industry, largely driven by the high incidence of periodontal diseases. Contributing factors include limited access to dental care, widespread tobacco use, and suboptimal oral hygiene practices.[31]

Key market drivers

The growth of the periodontal therapeutics market is primarily driven by rising awareness of oral health, a growing aging population, and continuous advancements in dental technology.[31]

Rising awareness of periodontal health

Rising awareness of oral health is one of the key drivers of growth in the periodontal therapeutics market. The WHO has played a major role in this effort, promoting prevention-focused strategies through global initiatives. In 2021, the WHO passed a resolution encouraging oral health promotion in families, schools, and workplaces and called for its integration into broader healthcare policies. Building on this, a global strategy was adopted in 2022 to ensure universal access to oral healthcare by 2030, with clear goals and monitoring frameworks. The 2022 Global Oral Health Status Report further emphasized the need for public health approaches targeting common risk factors, such as sugar consumption, tobacco use, and alcohol, and advocated for the integration of oral health into primary care and better access to essentials like fluoride toothpaste.[31]

Growth of the geriatric population

The rising geriatric population also significantly contributes to the growth of the periodontal therapeutics market. Age is a major contributing factor to both the onset and progression of periodontal disease, with its risk and incidence increasing significantly with advancing age.[34,35] More than 42% of adults over the age of 30 have some type of gum disease, with approximately 8% suffering from severe periodontitis. Among individuals aged 65 and above, the prevalence approaches 60%, highlighting the age-associated risk of periodontal disease progression. As of November 2023, the global population aged 65 and older is projected to double, increasing from approximately 800 million in 2022 to around 1.6 billion by 2050. This underscores the substantial burden of periodontal disease in older populations and the need for focused oral health strategies.[31]

Technological advancements in dentistry

Technological advancements in dentistry have greatly enhanced the diagnosis, treatment, and management of periodontal disease. For instance, as of July 2023, innovations in digital dentistry, particularly advanced imaging techniques, have enabled periodontists to create accurate 3D models of patients' mouths. These models improve the planning of procedures like dental implants, leading to greater precision, better communication among dental professionals, and improved patient outcomes. These technological advancements contribute to a higher diagnosis rate by enabling earlier and more precise detection of periodontal conditions, ultimately expanding the need for treatment solutions and fueling the growth of the periodontal therapeutics market.[31]

Market segmentation

To better understand this evolving landscape, the market can be segmented based on disease severity, type of drug, and distribution channels.[15,16]

By disease type

The disease segment of the periodontal therapeutics market is primarily divided into chronic periodontal disease and gingivitis.[36] In 2023, the chronic periodontal disease segment led the market with a 34.7% share. Chronic periodontitis, a progressive condition involving gum inflammation, tissue damage, and bone loss, is often linked to systemic illnesses such as diabetes, cardiovascular disease, respiratory infections, and chronic kidney disease. The bidirectional relationship between these chronic disorders and periodontitis highlights the need for integrated healthcare approaches and creates opportunities for businesses to offer holistic dental solutions that also address broader health concerns.[31]

Meanwhile, the gingivitis segment is projected to grow rapidly during the forecast period. Caused by bacterial plaque buildup, gingivitis affects over 90% of the global population at some level.

Despite its prevalence, many individuals delay or avoid treatment, which presents a strong opportunity for dental companies to expand public education efforts and promote preventive care. This could drive demand for related products and services in a largely untapped segment of the market. Improved oral hygiene habits, increased public awareness of early gum disease symptoms, and the wider availability of over-the-counter treatments that promote early intervention are also driving this growth.[31,36]

By drug type

The drug type segment of the periodontal therapeutics market is primarily categorized into doxycycline, chlorhexidine, minocycline, metronidazole, and other pharmaceutical agents. Doxycycline held the largest share of the periodontal therapeutics market in 2023, accounting for 37.7%, while minocycline is becoming the fastest-growing segment, as seen in Figure 2. Even at low concentrations, doxycycline has been shown to inhibit matrix metalloproteinase-8 (MMP-8), an enzyme that breaks down connective tissue and is highly prevalent in periodontitis. Additional research supports the efficacy of sub-antimicrobial doses of doxycycline in reducing pocket depth, enhancing clinical attachment level, and decreasing gingival inflammation.[31,36,37]

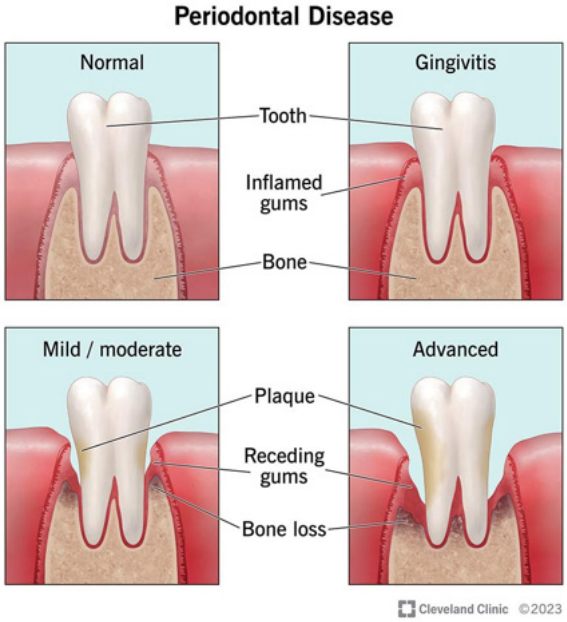

Figure 2 Illustration of periodontal disease progression.

The image shows the progression of periodontal disease, with the tooth, gums, and bone labeled.

The minocycline segment is expected to grow significantly during the forecast period. As a tetracycline-class antibiotic, minocycline is widely used for treating bacterial infections, like periodontal disease. A study published by the Multidisciplinary Digital Publishing Institute (MDPI) in April 2022 found that delivering minocycline directly to periodontal sites led to notable changes in the subgingival bacterial composition. This localized application contributes to improved therapeutic outcomes for patients with periodontitis, reinforcing its value in targeted periodontal treatments.

By distribution channel

The distribution channel segment of the periodontal therapeutics market is broadly categorized into hospital pharmacies, retail pharmacies, and online channels shown in Figures 3–5. In 2023, the hospital pharmacies segment accounted for the largest market share at 42.6%. These pharmacies play a vital role in delivering medications and periodontal treatments directly to patients within hospital settings. With growing awareness of the systemic links between oral health and overall health, hospitals are increasingly incorporating comprehensive oral care into their treatment protocols. Many are expanding dental services or establishing dedicated oral health clinics to manage the rising incidence of periodontal diseases. This expansion has driven greater demand for periodontal therapeutics through hospital pharmacies, which work closely with dental specialists like periodontists and oral surgeons to ensure effective medication management.[31]

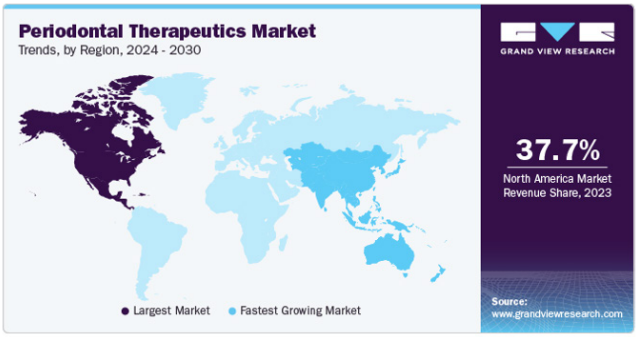

Figure 3 Infographic of the regional distribution of the periodontal therapeutics market.

The image shows the distribution of the global periodontal therapeutics market by region in 2023.

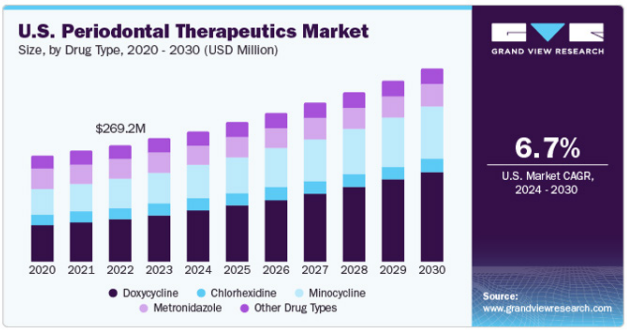

Figure 4 Infographic of the U.S. periodontal therapeutics market by drug type.

The image shows the United States periodontal therapeutics market segmented by drug type from 2020 to 2030.

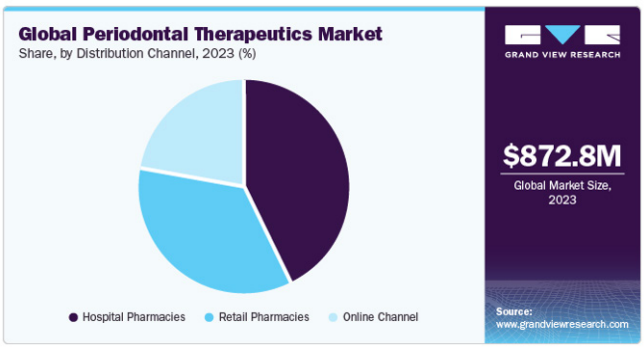

Figure 5 Infographic of the global periodontal therapeutics market by distribution channels.

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Retail pharmacies held the second-largest share of the market in 2023 and are rapidly emerging as the fastest-growing distribution channel. This growth is fueled by rising consumer demand for convenience and increased access to prescription-strength medications and preventive treatments in retail settings. These outlets contribute significantly by offering easy access to both over-the-counter and prescription periodontal therapeutics. Stocking a range of products, from antimicrobial mouth rinses to localized antibiotic treatments, retail pharmacies cater to individuals looking to manage or improve their oral health. Additionally, pharmacists often provide guidance on proper oral hygiene and medication use, positioning retail pharmacies as accessible hubs for oral health education and treatment.[31,36]

Furthermore, online channels provide a convenient platform for individuals to access periodontal treatments and medications, offering home delivery services and a wide selection of products that support both prescription and over-the-counter oral healthcare needs.[31]

Current therapeutic products and approaches

Approaches to periodontal disease treatment can be broadly classified into non-surgical and surgical interventions, antibiotic therapies, and regenerative materials.[38-42]

Non-surgical and surgical treatments

If periodontal disease is not advanced, treatment may involve less invasive non-surgical procedures, such as scaling and root planing. During this deep-cleaning procedure, the periodontist first removes plaque and bacterial deposits from beneath the gumline (scaling) (Figures 6–8), followed by smoothing the tooth roots (root planing) to discourage future plaque buildup and promote gum reattachment to the teeth.[4,38,43,44]

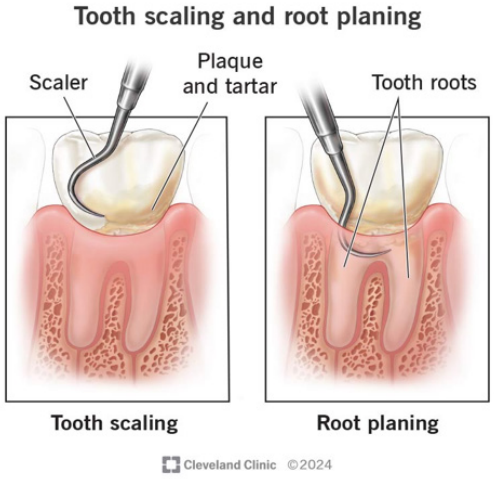

Figure 6 Illustration of tooth scaling and root planing procedure.

The image shows the procedure of tooth scaling and root planing, highlighting the removal of subgingival plaque and smoothing of root surfaces.

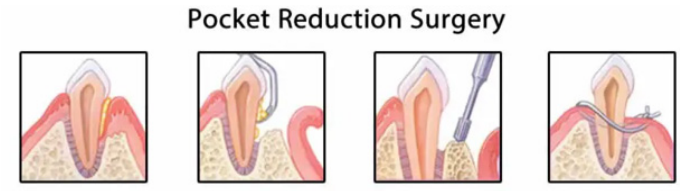

Figure 7 Illustration of pocket reduction surgery. From left to right: tartar buildup in a deep periodontal pocket, gum tissue is lifted and tartar is removed, underlying bone is smoothed and reshaped, and gum tissue is sutured back into place.

The image shows the steps of pocket reduction surgery. From left to right, the image depicts tartar accumulation in a deep periodontal pocket, elevation of the gum tissue and removal of tartar, smoothing and reshaping of the underlying bone, and suturing of the gum tissue back into place.

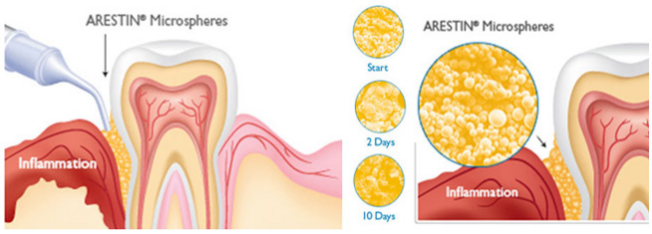

Figure 8 Illustration showing ARESTIN application (left) and its presence in the periodontal pocket after 10 days (right).

The image shows the application of ARESTIN is applied to an inflamed periodontal site and its presence within the pocket at baseline, day 2, and day 10, demonstrating sustained antibiotic release over time.

If periodontal disease has progressed to an advanced stage, surgical interventions may be required, including pocket reduction surgery or gum and bone grafting procedures. These surgeries aim to reduce deep periodontal pockets, restore damaged tissues, and support the regeneration of bone and gum structures. During a periodontal pocket reduction procedure, the periodontist carefully folds back the gum tissue to expose the tooth roots where normal scaling and root planing cannot reach and removes the bacteria that contribute to disease. If bone loss is present, the underlying bone may be reshaped to reduce areas where bacteria can accumulate, promoting better reattachment of the gum tissue and making it easier to maintain long-term oral health.[4,38,45,46]

Furthermore, if gum tissue has been lost due to periodontal disease, a periodontist may recommend gum graft surgery to cover exposed tooth roots, reduce further recession, and improve the appearance of your smile. This involves adding tissue, either from the roof of the patient's mouth or a licensed donor source, to the areas of gum loss to reinforce the gumline and promote healthier, more stable gums.

Similarly, when periodontitis leads to bone loss around a tooth root, a dental bone graft may be performed to restore the damaged area (Figures 9–11),. The graft, made from the patient's own bone, donated tissue, or synthetic material, serves as a scaffold to support natural bone regeneration and helps stabilize the tooth to prevent further loss.[4,38]

Figure 9 Illustration showing ATRIDOX application.

The image shows the application of ATRIDOX to a periodontal site.

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Figure 10 Illustration showing Straumann Emdogain application.

The image shows the application of Straumann Emdogain to a periodontal site.

Figure 11 Image of BioMend membranes.

The image shows the BioMend membranes in various sizes.

Antibiotic therapies

ARESTIN, a locally administered antibiotic containing minocycline, is widely used as an adjunctive therapy for the treatment of periodontal disease.[39,47] It is the only FDA-approved antibiotic specifically designed for local application alongside scaling and root planing in managing the condition. ARESTIN enhances clinical outcomes by delivering targeted antimicrobial microspheres directly into periodontal pockets to provide localized and sustained infection control. Clinical studies have shown that ARESTIN consistently reduces pocket depth at nine months, achieving nearly 20% greater reduction compared to scaling and root planing alone.[48]

ATRIDOX is a broad-spectrum antibiotic derived synthetically from oxytetracycline used to treat chronic adult periodontitis by promoting clinical attachment gain, reducing probing depth, and decreasing bleeding on probing. It is a subgingival controlled-release system delivered via a two-syringe mixing system. Syringe A contains a bioabsorbable polymer (ATRIGEL) composed of poly (DL-lactide) dissolved in N-methyl-2-pyrrolidone, while Syringe B contains doxycycline hyclate. When combined, the product forms a viscous liquid that solidifies upon contact with crevicular fluid, enabling a controlled release of doxycycline over seven days. Similar to ARESTIN, clinical results showed that ATRIDOX outperformed both the vehicle control and oral hygiene measures alone.[40,48-50]

Regenerative biomaterials

Straumann Emdogain is a gel composed of enamel matrix derivatives, primarily amelogenins, and is used to regenerate gum tissue in patients with periodontal disease. These proteins, which are derived from developing pig teeth, help mimic natural biological processes involved in tooth development, promote the regeneration of soft and hard tissues, and aid in the reformation of periodontal attachment. Emdogain enhances wound healing in oral surgical procedures by stimulating angiogenesis, regulating the production of inflammation-related factors, and exhibiting antimicrobial activity against oral pathogens. It has been shown to regenerate approximately 1 mm more tissue compared to surgical cleaning alone. Clinically, Emdogain delivers results comparable to guided tissue regeneration, but with the added advantages of easier application and fewer complications.[42,51,52]

BioMend and BioMend Extend are absorbable collagen membranes derived from bovine collagen, specifically designed for guided tissue regeneration (GTR) in periodontal defects. These membranes support the regeneration of the periodontal apparatus by acting as a barrier that prevents epithelial cell migration while allowing the passage of essential nutrients. BioMend membranes are resorbable, eliminating the need for a second surgical procedure for removal, which reduces wound trauma and surgical time. They also serve as a space-maintaining scaffold, promoting tissue regrowth in GTR and guided bone regeneration (GBR) procedures. The membranes are tear-resistant, suturable, and conform well to defect morphology, whether wet or dry. BioMend is typically absorbed within 8 weeks, while BioMend Extend lasts up to 18 weeks, offering clinicians flexibility based on the clinical need.[41,53]

Emerging therapies: products in clinical and pre-clinical development

A wide range of clinical and preclinical trials are currently underway to explore treatments for periodontal disease, spanning innovations from new toothpastes and antibiotics to advanced approaches like stem cell therapies (Table 1).[54-56]

Novel dentifrice formulations

A recent randomized, double-blind clinical trial published in the Journal of Periodontology investigated the effectiveness of a new toothpaste formulation containing 0.454% stannous fluoride and 2.6% ethylenediamine tetra acetic acid (EDTA) in reducing plaque and gingival inflammation, both of which are precursors to periodontal disease. Over a three-month period, participants using this innovative dentifrice experienced statistically significant reductions in whole-mouth plaque levels, gingival inflammation, and bleeding compared to those using other commercially available fluoride toothpastes. These findings suggest that incorporating this stannous fluoride and EDTA toothpaste into daily oral hygiene routines may enhance plaque control and gum health, potentially preventing the progression of periodontal disease.[54]

Targeted antibiotic therapies

Moreover, a recent preclinical study has identified FP-100 as a promising new antibiotic for the treatment of periodontal disease. Developed by scientists at the ADA Forsyth Institute in collaboration with Flightpath Biosciences, FP-100 is a narrow-spectrum antibiotic that specifically targets *Fusobacterium nucleatum*, a key pathogen implicated in the onset and progression of periodontitis, without

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disrupting beneficial oral or gut microbiomes. In both in vitro experiments and a mouse periodontitis model, FP-100 effectively eradicated *F. nucleatum*, leading to significant reductions in gum inflammation and bone loss associated with periodontal disease. Notably, this targeted approach minimizes the risk of antibiotic resistance and preserves the balance of the oral microbiome, addressing limitations of traditional broad-spectrum antibiotics. While these findings are promising, FP-100 has not yet undergone human clinical trials. Researchers emphasize the need for further studies to evaluate its safety and efficacy in humans before it can be considered for clinical use.[54,55]

Table 1 Summary of current therapeutic products and approaches in periodontal disease treatment

Approach	Product/method	Key components	Mechanism function	References
Non-surgical treatment	Scaling and root planing	Manual instruments	Removes subgingival plaque and smooths root surfaces to promote reattachment	4,38,43
Surgical treatment	Pocket reduction surgery	Surgical tools	Reduces deep pockets by lifting the gum tissue and cleaning root surfaces	4,38,45
	Gum graft surgery	Autografts or donor tissue	Covers exposed roots and reinforces the gum line	4,38,45
	Bone graft surgery	Autologous, allogenic, or synthetic materials	Provides a scaffold for new bone growth in areas of bone loss	4,38
Antibiotic therapy	ARESETIN	Minocycline microspheres	Locally administered antibiotic with sustained release in periodontal pockets	39,47,48
	ATRIDOX	Doxycycline in ATRIGEL polymer	Controlled release system that solidifies in the gingival crevice	40
Regenerative biomaterials	Straumann emdogain	Enamel matrix derivative (amelogenins) from porcine teeth	Promotes regeneration of soft/hard tissue	42,50
	Biomend/biomend expand	Resorbable bovine collagen membranes	Prevents epithelial migration while promoting bone and tissue regeneration	41, 53

Stem cell-based regenerative approaches

A 2023 systematic review and meta-analysis published in BMC Oral Health assessed the efficacy of stem cell-based therapies for periodontal regeneration. The researchers analyzed five randomized controlled trials involving 118 patients. This study found that treatments utilizing mesenchymal stem cells achieved better outcomes in clinical attachment level, pocket probing depth, and bone defect fill compared to conventional, cell-free therapies. These findings suggest that stem cell therapies can enhance the regeneration of periodontal structures such as bone, ligament, and connective tissue, offering potential benefits for patients with advanced periodontitis. However, the authors emphasize the need for further high-quality, large-scale clinical trials to confirm these results and to establish standardized treatment protocols (Table 2).[56]

Table 2 Summary of emerging clinical and preclinical therapeutic products for periodontal disease

Therapy type	Product	Stage	Key components	Mechanism	References
Advanced dentifrice	Stannous fluoride + EDTA	Clinical trial	0.454% stannous fluoride and 2.6% EDTA	Reduces plaque, gingival inflammation, and bleeding	54
Targeted antibiotic	FP-100	Preclinical	Narrow-spectrum antibiotic targeting *Fusobacterium nucleatum*	Selectively eliminates *F. nucleatum* while preserving beneficial microbiota	55
Stem cell therapy	Mesenchymal stem cells	Early clinical trials	Mesenchymal stem cells	Promotes the regeneration of periodontal tissues	56

Conclusion

Periodontal disease remains a prevalent global health concern, with significant implications for systemic health and quality of life.[3] Its well-established links to chronic illnesses, including cardiometabolic, neurodegenerative, autoimmune, and respiratory diseases, as well as certain cancers, highlight the need for a more integrated and multidisciplinary approach to prevention and treatment.[13-30]

The expanding market for periodontal therapeutics reflects both the urgent demand and substantial opportunity to enhance disease management through early detection, personalized treatment, and prevention.[3] Existing products have set the foundation for effective disease management, combining non-surgical and surgical procedures with pharmacological interventions and regenerative techniques.[38-42] Emerging therapies, ranging from novel antimicrobials and dentifrices

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to stem cell-based approaches, demonstrate a promising avenue that could redefine periodontal care.[54-56]

As the field moves forward, collaboration between industry, academia, and clinical practice will be essential to translate these advances into scalable, patient-centered solutions. Ultimately, the integration of next-generation technologies with current standards of care offers the potential to not only halt disease progression but also restore long-term oral and systemic health in a more personalized and durable manner.

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Conflicts of interest

The authors declare that there is no conflicts of interest.

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