Vol. 14, No. 4, July-August 2025

CONTEMPORARY TRENDS IN THE MANAGEMENT OF PERIODONTAL DISEASE AND ASSOCIATED INFECTIONS: IMPLICATIONS FOR ORAL HEALTH

Sorana Roșu [1], Marius Condur [2*], Gabriel Rotundu [2], Răzvan Gradinariu [2], Vlad Popovici [2], Alice Murariu [1], Florinel Cosmin Bida [3]

[1]"Gr. T. Popa" U.M.Ph. - Iași, Romania, Faculty of Dentistry, Department of Oral Health
[2]"Gr. T. Popa" U.M.Ph. - Iași, Romania, Faculty of Dentistry, Department of Periodontology
[3]"Gr. T. Popa" U.M.Ph. - Iași, Romania, Faculty of Dentistry, Department of Complete Dentures

*Corresponding author: Marius Condur e-mail: condur.marius@yahoo.com

ABSTRACT

Periodontal disease is among the most common chronic conditions worldwide, driven by microbial biofilm and host immune responses, and remains a major cause of tooth loss. Management has progressed from conventional mechanical and pharmacological methods to adjunctive, minimally invasive strategies. This narrative review highlights current antimicrobial approaches in periodontal therapy, focusing on photodynamic therapy, laser applications, systemic and local antibiotics, and controlled-release antiseptic systems. Photodynamic and laser therapies have demonstrated promising short-term clinical improvements, while clindamycin emerges as a valuable alternative due to its antimicrobial and immunomodulatory properties. Furthermore, slow-release chlorhexidine chips ensure sustained subgingival antibacterial effects, enhancing outcomes of scaling and root planning. Despite encouraging evidence, clinical variability and limited long-term data warrant further high-quality trials. Current antimicrobial strategies, when integrated with conventional debridement, can optimize infection control and contribute to personalized, sustainable periodontal care.

Key words: oral health, periodontal therapy, periodontal disease, bone loss, gingival recession, etc.

1. INTRODUCTION

Periodontal disease is one of the most prevalent chronic conditions worldwide, affecting up to 50–60% of the adult population and exerting a substantial impact on oral health and overall quality of life [1,2]. Clinically, it is characterized by gingival inflammation, progressive loss of supporting bone, and, in advanced stages, tooth loss [3]. The disease results primarily from the accumulation of bacterial biofilm and the host's immune-inflammatory response to pathogenic microorganisms [4].

Over the past decades, the management of periodontal disease has evolved considerably, shifting from conventional, non-specific interventions to more individualized strategies grounded in a detailed understanding of disease etiology and pathogenesis [5,6]. These advances have been driven by the growing recognition of the multifactorial nature of periodontal disease and the need for therapeutic approaches tailored to specific patient profiles [7].

At the same time, the global rise of antibiotic resistance [8] and the increasing demand for minimally invasive and sustainable treatments [9] have reshaped current clinical practice. Emerging therapeutic trends now focus on innovation and precision, emphasizing targeted antimicrobial strategies, host-modulation therapies, and the integration of novel technologies into periodontal care [10,11]. This paradigm shift underscores the importance of a deeper understanding of pathogenic mechanisms, host–microbe interactions, and environmental influences in disease progression [12].

The present paper aims to provide an updated

synthesis of current trends in the infectious management of periodontal disease, with particular emphasis on pharmacological innovations, targeted drug delivery systems, and adjunctive modalities such as photodynamic therapy and tissue bioengineering [13–15]. Moreover, the role of early diagnosis and personalized monitoring will be highlighted as key factors in optimizing clinical outcomes and promoting sustainable oral health [16].

2.LITERATURE REVIEW

Contemporary therapeutic trends increasingly emphasize precision medicine, incorporating advanced diagnostic tools, novel pharmacological agents, and innovative delivery systems to target periodontal pathogens more effectively while modulating the host response [16,17].

Adjunctive modalities—such as antimicrobial photodynamic therapy, laser-assisted approaches, and regenerative bioengineering techniques—are also gaining prominence for their potential to enhance clinical outcomes and promote long-term periodontal stability [18–20].

By exploring current innovations in pharmacology, targeted antimicrobial delivery, adjunctive therapies, and personalized monitoring, we provide an updated perspective on the evolving landscape of periodontal care and its potential to improve both oral and systemic health outcomes.

► ***photodynamic therapy***

Unlike other methods of tissue and cell destruction, photodynamic therapy (PDT) is both noninvasive and highly specific. It is based on the principle that a photosensitizer (PS), molecular oxygen, and visible or near-infrared (NIR) light must be simultaneously present, although none of these components alone is lethal or harmful to cells or tissues.

The photodynamic response may occur through two major processes, both of which rely significantly on molecular oxygen within living cells. These processes share the same initial phase.

After entering the cell, a photosensitizer absorbs photons at a specific wavelength corresponding to its absorption spectrum (AS), causing it to transition from its ground singlet state to an excited singlet state (S0 to S1). While part of the energy is lost as fluorescence, the remainder is used to promote the photosensitizer molecule to its active triplet state.

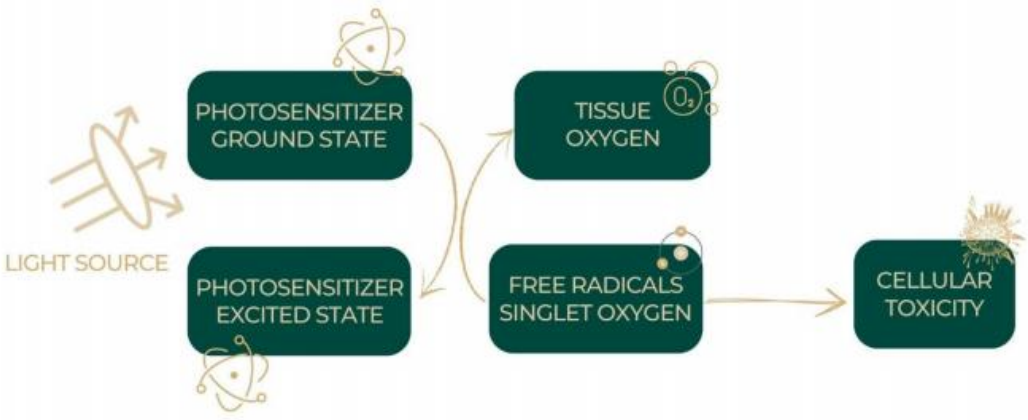

Fig 1. *Mechanism PDT* [21].

Xu and colleagues found that a 5-minute exposure to 665 nm laser light at 20 and 40 mW/cm² was sufficient to eliminate endodontic bacteria *in vitro*. Gingival fibroblasts and osteoblasts showed no apoptotic changes following laser therapy, indicating the safety and effectiveness of photodynamic therapy (PDT) [21].

Numerous studies have demonstrated that PDT is an effective adjunct to scaling and root

planing in the treatment of aggressive periodontitis. Adolescents are more susceptible to developing localized aggressive periodontitis, a rare condition. Zambon and colleagues observed that the subgingival microbiota of young patients with periodontitis exhibited higher concentrations of *Aggregatibacter actinomycetemcomitans* [22].

Park and collaborators demonstrated the feasibility of PDT mediated by Toluidine Blue O (TBO) as a noninvasive adjunctive method for the treatment of periodontitis [23]. *In vitro* investigations have shown that many microbes, including oral microorganisms, can be inactivated by PDT. Periodontal pathogens such as *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, *Fusobacterium nucleatum*, *Prevotella intermedia*, and *Streptococcus sanguis* were strongly inhibited by PDT under different conditions.

PDT demonstrated selectivity against periodontal pathogens without affecting the growth of resident oral bacteria. Its cytotoxic impact on normal periodontal cells was lower than that commonly observed with antiseptics. The use of antimicrobial PDT represents a promising alternative as it eliminates the need for standard drug therapy, shortens treatment duration, and prevents prolonged administration or excessive drug dosing. The combination of phototherapy with nystatin has been designed to drastically reduce colony counts compared with the use of the antifungal agent alone. Due to PDT-induced alterations, nystatin can penetrate fungal cells more effectively and bind to ergosterol in their membranes, resulting in cellular destruction and necrosis [24].

Although traditional medicine has historically prioritized pharmacological and surgical treatment methods, light-based therapy across the full spectrum has emerged as a credible alternative and is now employed in a variety of clinical contexts.

The integration of diagnostic and therapeutic light-based procedures is also considered a promising area for future development. Over the next decade, it is anticipated that multiple light technologies will become integral components of modern dental practice [25].

For the elimination of bacteria from supragingival and subgingival plaque, antimicrobial photodynamic therapy has been applied using various combinations of lasers and photosensitizing agents. In antimicrobial photodynamic therapy, specific photosensitizers employed include Toluidine Blue O [tolonium chloride: (7-amino-8-methyl-phenothiazin-3-ylidene)-dimethyl-ammonium ($C15H16N3S^+$)], Methylene Blue [3,7-bis(dimethylamino)phenazathionium chloride of tetramethylthionine ($C16H18N3ClS$) or phenothiazine-5-ium, 3,7-bis(dimethylamino) chloride], erythrosine, chlorin e6, and hematoporphyrin, all of which have been demonstrated to be safe when applied in medical settings [26].

With regard to antimicrobial photodynamic therapy, Methylene Blue and Toluidine Blue O have been shown to be highly effective photosensitizing agents for the inactivation of both gram-positive and gram-negative periodontopathogen bacteria.

However, differences exist in the susceptibility of gram-positive and gram-negative bacteria to treatment. Anionic and neutral photosensitizers have been reported to be effective against gram-positive bacteria; nevertheless, they are often ineffective against gram-negative bacteria [27]. Although still a subject of debate, gram-negative organisms appear generally more resistant to photodynamic therapy than gram-positive species, mainly due to structural differences in their outer membranes.

Gram-positive species possess a relatively porous cytoplasmic membrane that allows the photosensitizer to enter the cell. In contrast, gram-negative species have an additional outer membrane with a characteristic structure that serves as an effective permeability barrier, inhibiting the penetration of host cellular and humoral defense factors and conferring resistance to many antibiotics. Consequently, the outer membrane may reduce or prevent photosensitizer uptake [28].

Nonetheless, photosensitizers such as Toluidine Blue O and Methylene Blue, which possess a pronounced cationic charge, have

been shown to bind to the outer membrane of gram-negative bacteria and penetrate bacterial cells, exhibiting a high degree of selectivity for microbial killing compared with host mammalian cells [29].

Therefore, Toluidine Blue O and Methylene Blue have become the preferred photosensitizers in the treatment of periodontitis and peri-implantitis. However, Toluidine Blue O appears to demonstrate a greater capacity for killing both gram-positive and gram-negative bacteria compared with Methylene Blue.

At present, however, the light sources with specific wavelengths most commonly applied in photodynamic therapy are helium–neon lasers (633 nm), gallium–aluminum–arsenide diode lasers (630–690, 830, or 906 nm), and argon lasers (488–514 nm), whose wavelengths range from the visible blue spectrum of argon lasers to the red region of helium–neon and gallium–aluminum–arsenide lasers, extending into the infrared range of certain diode lasers [30].

High-energy laser irradiation is not employed to activate the photoactive dye, since relatively low exposures are sufficient to produce a high bactericidal effect. Several types of laser devices have been tested in *in vitro* research studies. However, in *in vivo* and clinical investigations, diode lasers remain the predominant light source utilized. Although Toluidine Blue O has generally been selected as the preferred photosensitizer in earlier *in vitro* studies, Methylene Blue has been used primarily in clinical studies, as commercial photodynamic therapy kits containing Methylene Blue are already available (Periowave™; Ondine Biopharma Corporation, Vancouver, Canada) and (Helbo; Photodynamic Systems GmbH & Co. KG, Grieskirchen, Austria) [31].

Non-laser light sources, such as light-emitting diodes (LEDs), have also been proposed as novel light activators in photodynamic therapy, since LED devices are more compact and portable, and their cost is considerably lower compared to traditional lasers.

Ezber and colleagues randomly assigned a total of ten patients to receive repeated applications of scalling and root planning, combined with photodynamic therapy (methylene blue – 30 mW diode laser), scaling and root planing alone, photodynamic therapy alone, and supragingival oral hygiene instructions. Methylene blue served as the photosensitizer and was applied in the form of a mouth rinse. Scaling and root planning were performed on days 1 and 7, while the laser was repeatedly applied over each papillary region (not into the periodontal pockets) on days 1, 2, 4, 7, 9, and 11. After 32 days of healing, significant clinical and microbiological improvements were observed only in the groups that received scaling and root planning in combination with photodynamic therapy, as well as scaling and root planning alone[32].

In contrast, improvements following photodynamic therapy alone, as well as in patients who received only oral hygiene instructions, did not reach statistical significance. Regarding the laser treatment, no complaints (such as discomfort, sensitivity, or pain) were reported by the subjects immediately after therapy or at 3 weeks of post-treatment.

The authors concluded that antimicrobial photodynamic therapy did not provide additional microbiological or clinical benefits beyond those achieved with conventional mechanical debridement. The reduced effect of photodynamic therapy in this study may be attributable to the indirect application of the therapy from the external gingival surface [32].

Fig. 2. *Clinical application of antimicrobial photodynamic therapy in the treatment of periodontitis (after Martu et al., 2019).*

Two randomized controlled clinical trials have evaluated the short-term clinical effects (up to 3 months) of adjunctive antimicrobial photodynamic therapy in combination with scaling and root planning in patients with chronic periodontitis.

Özberk and colleagues, using a three-arm parallel design, compared the efficacy of antimicrobial photodynamic therapy with that of scaling and root planning for the non-surgical treatment of moderate to advanced periodontal disease [33].

A total of 33 patients were assigned to receive either photodynamic therapy alone (methylene blue – 50 mW diode laser), scaling and root planning alone, or scaling and root planning combined with photodynamic therapy. Clinical assessments of bleeding on probing, probing pocket depth, and clinical attachment level were performed. After three months of healing, it was observed that the combination of scaling, root planning, and photodynamic therapy led to significant improvements in the investigated parameters compared with scaling and root planning alone at all evaluation points.

Karkhanechi et al. evaluated the effect of adjunctive antimicrobial photodynamic therapy (methylene blue – 100 mW diode laser) in chronic periodontitis using a split-mouth design [34]. A total of 20 patients underwent scaling and root planning, and sites were randomly assigned to receive additional photodynamic therapy. After irrigation and a 3-minute residence time, the residual photosensitizer was activated for 10 seconds per site (six sites in total). After 3 months of healing, the adjunctive use of photodynamic therapy resulted in significantly greater changes in mean relative clinical attachment level, probing pocket depth, gingival crevicular fluid flow rate, and bleeding on probing at sites that received photodynamic therapy compared with sites that received scaling and root planning alone.

Only one study, conducted by de Oliveira et al., reported the outcomes of antimicrobial photodynamic therapy as a monotherapy for the treatment of aggressive periodontitis. A total of 10 patients were randomly assigned, according to a split-mouth design, to receive either photodynamic therapy (methylene blue – 60 mW diode laser) or scaling and root planning [35]. The laser was applied for 10 seconds per site after a 3-minute residence time of the photosensitizer. Three months later, both treatment procedures resulted in comparable clinical outcomes, as evidenced by reductions in probing pocket depth and

gains in clinical attachment level, suggesting a potential clinical effect of photodynamic therapy as an alternative to scaling and root planning. In both groups, beneficial effects were pronounced in initially moderate and shallow pockets [36].

Overall, the available data from controlled clinical studies indicate that, in patients with chronic periodontitis, the adjunctive use of antimicrobial photodynamic therapy in combination with scaling and root planning may, in the short term (up to 3 or 6 months), lead to greater reductions in bleeding on probing compared with scaling and root planning alone (as observed in three studies), and greater reductions in probing pocket depth and gains in clinical attachment level compared with scaling and root planning alone (in two studies).

Since antimicrobial photodynamic therapy can be applied topically, the systemic administration of antibiotics may be avoided in the treatment of localized infections. In antimicrobial photodynamic therapy, a high concentration of the chemical agent at the infection site enables effective bacterial elimination without generating adverse effects on the patient's tissues. Multiple sessions of photodynamic therapy may enhance healing outcomes and improve its long-term effects [37].

However, it has not yet been established how frequently photodynamic therapy should be applied to efficiently eradicate bacteria and to prevent recolonization of previously treated sites following unsupervised periodontal therapy. Another adjunctive method that has been recently proposed in the literature is the use of probiotics, either systemically or locally, and future studies should compare these two adjunctive strategies in order to assess their relative efficacy.

► ***Laser Therapy***

Alternatively, irradiation with a diode laser represents a similar method, but it acts through different biochemical and biophysical mechanisms. Unlike photodynamic therapy, it does not require a photosensitizing agent; rather, the therapeutic effect is achieved through the intrinsic interactions between light radiation, periodontopathogenic bacteria, and host tissue [38].

Low-level laser therapy (LLLT) has been shown to enhance mitochondrial adenosine triphosphate production, thereby facilitating fibroblast proliferation, the release of growth factors, and collagen synthesis. At the same time, *in vitro* and animal studies have revealed that this therapy suppresses periodontal tissue inflammation by modulating the local immune response and reducing the production and release of certain pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and prostaglandin E2. Furthermore, it has been reported to improve local microcirculation through angiogenesis and vasodilation, thereby alleviating tissue edema and inflammation [39].

Although recent studies in literature have analyzed the effects of both laser therapy and photodynamic therapy in periodontal disease, the mechanisms underlying bacterial eradication remain insufficiently explored. Moreover, to date, no study has examined the effect of diode laser therapy and photodynamic treatment on a periodontopathogen in the context of anti-TNF-α immunomodulatory therapy[40].

Considering the immunocompromised status of certain patients undergoing immunosuppressive therapy and the potential drug interactions associated with systemically administered antimicrobial agents, the investigation of local, minimally invasive methods for inactivating periodontal pathogens in the setting of systemic immune-modifying treatments, such as anti-TNF-α agents, is well justified [41].

Technique	Bacteria	Effect	Author
PDT + toluidine or methylene blue dye	*A. actinomycetemcomitans*	100% eradication at 10 mg/mL	Valle et al., 2019 [14]
PDT + rose bengal	*P. gingivalis*, *A. actinomycetemcomitans*, *F. nucleatum*	Maximal reduction at 160 µg/mL rose bengal	Wang et al., 2021 [15]
Diode Laser 810-nm	*A. actinomycetemcomitans*	93% reduction at 2.5 W; 30 s	Tantivitayakul et al., 2018 [16]
Diode laser 635 nm + phycocyanin	*P. gingivalis*	Mean reduction 44.24%	Etemadi et al., 2022 [17]

Table 1. *Studies Investigating the Effect of Laser Therapy and Photodisinfection on Periopathogenic Bacteria In Vitro*

LASER is an acronym for *Light Amplification via the Stimulated Emission of Radiation*. Since Maiman first introduced the use of lasers in dentistry in the 1960s, researchers have explored their numerous potential clinical applications. Soft or cold lasers, based on semiconductor diode devices, are compact and cost-effective instruments predominantly used in clinical practice, whereas hard lasers, such as carbon dioxide (CO_2), neodymium-doped yttrium aluminum garnet (Nd:YAG), and erbium-doped yttrium aluminum garnet (Er:YAG), provide applications in both hard and soft tissues, but their widespread use is limited due to high costs and the potential for thermal damage [42].

Dental lasers deliver light to tissues through an active medium, which may be a gas, a crystal, or a solid semiconductor. This active medium is the principal factor determining the laser's wavelength and other physical properties.

The carbon dioxide (CO_2) laser has a wavelength that is highly selective for water in tissues, enabling the rapid and efficient removal of soft tissue while simultaneously achieving hemostasis with minimal penetration [43].

Soft tissue surgery is best performed using the CO_2 laser (10,600 nm), the Nd:YAG laser (1064 nm), the diode laser (DL; 800–980 nm), the Er:YAG laser (2940 nm), or the Er,Cr:YSGG laser (2780 nm). In addition to being a highly conservative technique, its benefits include an increase in tissue temperature, which aids hemostasis and reduces microbial growth.

The neodymium-doped yttrium aluminum garnet (Nd:YAG) laser is considered a highly efficient surgical laser because its wavelength is well absorbed by pigmented tissues. Beyond its surgical applications, research has also investigated the use of Nd:YAG lasers for non-surgical sulcular debridement in the management of periodontal disease [44].

Erbium family lasers are available in two variants: one with a longer wavelength (Er,Cr:YSGG; yttrium–scandium–gallium–garnet) and the other with a shorter wavelength (Er:YAG; yttrium–aluminum–garnet). Among all dental lasers, erbium lasers exhibit the highest absorption in water and the strongest affinity for hydroxyapatite, making them the preferred choice for the restoration of hard dental tissues. *In vitro* investigations have demonstrated that both Er:YAG and Er,Cr:YSGG lasers cause alterations in the morphology of treated root surfaces, resulting in greater surface roughness and irregularity [45].

Diode lasers generate wavelengths in the range of 810–980 nm using a solid-state semiconductor active medium composed of aluminum, gallium, arsenide, and, in some cases, indium. Esthetic gingival recontouring, soft tissue crown lengthening, exposure of teeth impacted by soft tissue, removal of inflamed or hypertrophic tissue, frenectomies, and photo stimulation of aphthous or herpetic lesions are just a few examples of procedures in this category .

For non-invasive periodontal therapy, dentists may employ a combination of diode lasers (808–904 nm), neodymium-doped yttrium aluminum garnet lasers (Nd:YAG; 1064 nm), erbium-doped yttrium aluminum garnet lasers (Er:YAG; 2940 nm), and erbium–chromium lasers.

► *Clindamycin – An Alternative Treatment Option in Periodontal Disease*

Clindamycin is an antibiotic originally derived from lincomycin, with a broad spectrum of

action and high activity against gram-positive aerobic bacteria as well as a wide range of anaerobic bacteria, including β-lactamase–producing pathogens. *In vitro* and *in vivo* studies have demonstrated that this drug achieves high concentrations at the site of infection, reducing bacterial virulence while enhancing the phagocytic activity of host lymphocytes. When administered orally, clindamycin is absorbed rapidly and efficiently, and its concentration remains at an optimal level to inhibit microbial growth for at least six hours. It has proven highly effective in penetrating the supporting periodontium [46].

In addition, it may be administered intravenously, showing remarkable tissue distribution and increased efficacy in infections caused by *Staphylococcus aureus*.

Clindamycin is also suggested to exert immunomodulatory properties through the suppression of pro-inflammatory cytokine release and its effects on phagocyte function, which has been considered superior to dexamethasone in the context of *Porphyromonas gingivalis*. Furthermore, clindamycin induces morphological alterations on bacterial surfaces to facilitate their destruction and stimulates chemotaxis, thereby promoting the mobilization of polymorphonuclear leukocytes to the infection site and enhancing bacterial phagocytosis [47].

Because clindamycin has a relatively short half-life, it requires administration every six hours to maintain adequate antibiotic concentrations. This review highlights the use of clindamycin as an alternative option in the treatment of periodontal disease within the context of currently available antibiotic and antimicrobial therapies and their modes of administration [48].

Clindamycin exerts its bacteriostatic effect by inhibiting microbial protein synthesis through binding to bacterial RNA at the 50S ribosomal subunit. In addition to its direct antibacterial effect via ribosomal targeting, clindamycin possesses several unique pharmacological properties that enhance its clinical efficacy.

It also inhibits bacterial proteins, enzymes, cytokines, and toxins, such as those produced by *Clostridium* species and *Staphylococcus aureus*.

Its ability to accumulate intracellularly within neutrophil organelles via the nucleoside transport system, and to promote intracellular bacterial killing, has been attributed to a proposed synergistic effect between clindamycin and neutrophils in oxidative eradication mechanisms [49].

Clindamycin further suppresses the release of pro-inflammatory cytokines such as TNF-α and IL-1β, which, when excessively secreted by bacteria and neighboring host cells, contribute to additional destruction of periodontal tissues. Thus, the reduction of TNF-α and of the chemokine CXCL-1 represents another mechanism mediating the inhibitory effect of clindamycin in inflammatory conditions such as periodontitis [50].

Advantages	Disadvantages
Can be administered in a multitude of formulations, both locally and systemically	Primary adverse effects of clindamycin with systemic administration are allergic reactions, pseudomembranous colitis, nausea, vomiting, and diarrhea
Efficiency is not affected by diet	Cannot be administered to patients with a history of pseudomembranous colitis or ulcerative colitis or to pregnant persons
Active against most aerobic Gram-positive, anaerobic Gram-positive and Gram-negative bacteria	Aerobic Gram-negative bacilli are usually resistant due to poor permeability of the cellular outer envelope
Active against most periodontopathogenic bacteria (*Actinomyces, Eubacterium, Bacteroides, Prevotella, Porphyromonas, Fusobacterium, Veillonella* spp.)	Involved in antibiotic-associated diarrhea due to *Clostridium difficile* overgrowth
Reduces adherence of bacteria to host cells, increases intracellular killing of susceptible organisms	Can cause taste disorders, oesophagitis and changes in hematological parameters
Good penetration inside supporting periodontium	Mechanisms of antibiotic resistance: bacterial cell impermeability, target site alteration, enzymatic alteration or destruction of the antibiotic, increased efflux
Does not block the proangiogenic activity, thus having positive effect in the overall regenerative outcome	Insufficiently researched in clinical trials regarding periodontal disease activity in comparison to other more popular antibiotic regimens

Table 2. *Advantages and Disadvantages of Clindamycin Use*
(After Luchian et al., 2022)

► Chlorhexidine – Slow-Release Systems

The role of supragingival scaling, as well as subgingival scaling and root planning (SRP), is crucial in periodontal therapy. In recent years, increasing emphasis has been placed on optimizing these therapeutic procedures through the adjunctive use of additional products to enhance the efficacy of SRP. Chlorhexidine gluconate represents a reliable antiseptic option that can be combined with SRP to reduce probing depth (PD) [50,51].

Van der Ouderaa previously described the ideal antimicrobial properties required for the control of periodontal disease, and chlorhexidine possesses most of these characteristics. Thus, a local delivery system for chlorhexidine, in conjunction with conventional therapy, may control the progression of periodontal disease more effectively. Previous studies have demonstrated that the use of **PerioChip** maintains a chlorhexidine concentration of over 125 mg/ml for 7–10 days in the gingival crevicular fluid—sufficient to eliminate more than 99% of subgingival microorganisms in periodontal pockets [52.53].

The use of local antimicrobial delivery systems should not replace the necessity for thorough SRP, which remains the most important and primary modality of treatment.

PerioChip is a biodegradable chip used for reducing periodontal pocket depth in patients with periodontitis and pockets ≥5 mm, when used as an adjunct to scaling and root planing (SRP). Its use not only reduces the bacterial load of periodontal pockets but also limits recolonization. This may be achieved by reducing the virulence of certain periodontal pathogens through inhibition of their proteolytic and glycosidic activities, as these activities contribute to the production of potential virulence factors [54-56].

Clinical findings have demonstrated reductions in both studied parameters—periodontal pocket depth and bleeding index—following treatment with Glucosite gel as well as PerioChip. The most significant

improvements were observed in Group C, treated with SRP and PerioChip.

3.FUTURE PERSPECTIVES

The future of periodontal infection management lies in the integration of advanced, minimally invasive, and personalized approaches that move beyond conventional pharmacological and mechanical methods. Emerging trends emphasize the application of nanotechnology-based drug delivery systems, which provide controlled, site-specific release of antimicrobial agents directly into periodontal pockets.

Such platforms enhance drug bioavailability, prolong therapeutic action, and significantly reduce systemic exposure, thereby minimizing the risk of adverse effects and antimicrobial resistance. Parallel to these innovations, there is growing interest in the use of probiotics and microbiome-modulating therapies, aiming not only to suppress periodontal pathogens but also to restore microbial homeostasis within the oral cavity.

By reshaping the subgingival ecosystem and strengthening host defences, these approaches seek to promote long-term stability rather than transient bacterial reduction. Together, nanotechnology-driven therapeutics and microbiome-focused strategies exemplify a paradigm shift toward precision medicine in periodontology, where disease management is tailored to individual microbial profiles, host immune responses, and overall systemic health.

Artificial intelligence (AI) and digital technologies are expected to play a transformative role in the diagnosis, risk assessment, and treatment planning of periodontal disease. Advanced algorithms, integrating data from clinical imaging, salivary biomarkers, and genomic sequencing, may allow for real-time stratification of patients according to disease susceptibility and therapeutic response.

Such predictive models could support clinicians in designing personalized, evidence-based protocols while also facilitating early intervention and long-term monitoring. Beyond diagnostics, AI-driven decision-support tools hold the potential to optimize chairside efficiency, standardize outcomes, and reduce human error in clinical practice.

In parallel, regenerative medicine is opening new horizons for periodontal therapy. Tissue engineering strategies employing biomimetic scaffolds, bioactive molecules, and stem cell–based approaches aim not only to repair but to fully regenerate lost periodontal structures, including cementum, periodontal ligament, and alveolar bone.

The integration of growth factor–enriched matrices and gene-editing technologies could further enhance the regenerative potential, shifting the therapeutic goal from disease control to the restoration of full oral functionality. As these innovations mature, they are anticipated to redefine the standard of care, bridging the gap between infection control and true functional rehabilitation of periodontal tissues.

In the broader context of global health, reducing antibiotic resistance remains a critical priority. Consequently, antimicrobial photodynamic therapy, laser-assisted protocols, and controlled-release antiseptic systems may become increasingly valuable as non-antibiotic alternatives. Long-term, well-designed randomized controlled trials are necessary to validate these innovative strategies and establish evidence-based guidelines for their routine integration into periodontal practice.

4. CONCLUSIONS

- ✓ Periodontal disease remains a highly prevalent chronic condition with significant implications for oral health and systemic well-being. Despite the effectiveness of conventional approaches

such as scaling and root planing, as well as adjunctive pharmacological interventions, these strategies are often limited by issues such as bacterial recolonization, antimicrobial resistance, and incomplete tissue regeneration.

- ✓ Recent advances in antimicrobial photodynamic therapy, laser applications, controlled-release antimicrobial systems, and alternative antibiotics such as clindamycin highlight the ongoing shift toward therapies that are targeted, minimally invasive, and patient-centered.
- ✓ Furthermore, the integration of emerging technologies, including nanotechnology, microbiome modulation, and digital innovations such as artificial intelligence, illustrates a clear paradigm shift from a purely infection-control model to one that emphasizes precision, personalization, and long-term sustainability.
- ✓ Ultimately, the future of periodontal infection management is defined by an interdisciplinary approach that combines advanced biomedical research with clinical innovation. By aligning antimicrobial strategies with regenerative medicine and individualized patient care, clinicians will be better equipped to preserve oral health, prevent disease recurrence, and contribute to overall systemic health optimization.

REFERENCES

1. Tonetti, M.S.; Jepsen, S.; Jin, L.; Otomo-Corgel, J. Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action. *J. Clin. Periodontol.* **2017**, *44*, 456–462.
2. Peres, M.A.; Macpherson, L.M.D.; Weyant, R.J.; Daly, B.; Venturelli, R.; Mathur, M.R.; Listl, S.; Celeste, R.K.; Guarnizo-Herreño, C.C.; Kearns, C.; et al. Oral diseases: A global public health challenge. *Lancet* **2019**, *394*, 249–260.
3. Preshaw, P.M.; Alba, A.L.; Herrera, D.; Jepsen, S.; Konstantinidis, A.; Makrilakis, K.; Taylor, R. Periodontitis and diabetes: A two-way relationship. *Diabetologia* **2012**, *55*, 21–31.
4. Kinane, D.F.; Chestnutt, I.G. Smoking and periodontal disease. *Crit. Rev. Oral Biol. Med.* **2000**, *11*, 356–365.
5. Taba, M., Jr.; Souza, S.L.; Mariguela, V.C. Periodontal disease: A genetic perspective. *Braz. Oral Res.* **2012**, *26*, 32–38.
6. Pólvora, T.L.S.; Nobre, Á.V.V.; Tirapelli, C.; Taba, M., Jr.; Macedo, L.D.; Santana, R.C.; Pozzetto, B.; Lourenço, A.G.; Motta, A.C.F. Relationship between human immunodeficiency virus (HIV-1) infection and chronic periodontitis. *Expert Rev. Clin. Immunol.* **2018**, *14*, 315–327.
7. Shapira, L.; Wilensky, A.; Kinane, D.F. Effect of genetic variability on the inflammatory response to periodontal infection. *J. Clin. Periodontol.* **2005**, *32*, 72–86.
8. Marsh, P.D. Dental plaque: Biological significance of a biofilm and community life-style. *J. Clin. Periodontol.* **2005**, *32*, 7–15.
9. Berezow, A.B.; Darveau, R.P. Microbial shift and periodontitis. *Periodontology 2000* **2011**, *55*, 36–47.
10. Mombelli, A. Microbial colonization of the periodontal pocket and its significance for periodontal therapy. *Periodontology 2000* **2018**, *76*, 85–96.
11. Feres, M. Antibiotics in the treatment of periodontal diseases: Microbiological basis and clinical applications. *Ann. R. Australas. Coll. Dent. Surg.* **2008**, *19*, 37–44.
12. Butera, A.; Gallo, S.; Maiorani, C.; Molino, D.; Chiesa, A.; Preda, C.; Esposito, F.; Scribante, A.

Probiotic Alternative to Chlorhexidine in Periodontal Therapy: Evaluation of Clinical and Microbiological Parameters. *Microorganisms* **2020**, *9*, 69.

13. Butera, A.; Gallo, S.; Pascadopoli, M.; Luraghi, G.; Scribante, A. Ozonized Water Administration in Peri-Implant Mucositis Sites: A Randomized Clinical Trial. *Appl. Sci.* **2021**, *11*, 7812.
14. Valle, P.A.; Coria, L.N.; Plata, C.; Salazar, Y. CAR-T Cell Therapy for the Treatment of ALL: Eradication Conditions and In Silico Experimentation. *Hemato* **2021**, *2*, 441-462.
15. Wang B, Wang JH, Liu Q, Huang H, Chen M, Li K, Li C, Yu XF, Chu PK. Rose-bengal-conjugated gold nanorods for in vivo photodynamic and photothermal oral cancer therapies. Biomaterials. 2014 Feb;35(6):1954-66.
16. Tantivitayakul P, Rassameemasmaung S, Thapanabhiboonsuk S. *In vitro* effect of diode laser against biofilm of *Aggregatibacter actinomycetemcomitans*. Eur J Dent. 2018 Oct-Dec;12(4):485-490.
17. Etemadi, A.; Khajehmougahi, K.; Solimei, L.; Benedicenti, S.; Chiniforush, N. Photobiomodulation Effect of Different Diode Wavelengths on the Proliferation of Human Buccal Fat Pad Mesenchymal Cells. *Appl. Sci.* **2024**, *14*, 847.
18. Giuroiu, C.L.; Andrian, S.; Stoleriu, S.; Scurtu, M.; Țănculescu, O.; Poroch, V.; Sălceanu, M. The Combination of Diode Laser and Ozonated Water in the Treatment of Complicated Pulp Gangrene. *Appl. Sci.* **2020**, *10*, 4203.
19. Silva, V.; Peirone, C.; Capita, R.; Alonso-Calleja, C.; Marques-Magallanes, J.A.; Pires, I.; Maltez, L.; Pereira, J.E.; Igrejas, G.; Poeta, P. Topical Application of Ozonated Oils for the Treatment of MRSA Skin Infection in an Animal Model of Infected Ulcer. *Biology.* **2021**, *10*, 372.
20. Di Mauro, R.; Cantarella, G.; Bernardini, R.; Di Rosa, M.; Barbagallo, I.; Distefano, A.; Longhitano, L.; Vicario, N.; Nicolosi, D.; Lazzarino, G.; et al. The Biochemical and Pharmacological Properties of Ozone: The Smell of Protection in Acute and Chronic Diseases. *Int. J. Mol. Sci.* **2019**, *20*, 634.
21. Luchian, I.; Budală, D.G.; Baciu, E.-R.; Ursu, R.G.; Diaconu-Popa, D.; Butnaru, O.; Tatarciuc, M. The Involvement of Photobiology in Contemporary Dentistry—A Narrative Review. *Int. J. Mol. Sci.* **2023**, *24*, 3985.
22. Monzillo, V.; Lallitto, F.; Russo, A.; Poggio, C.; Scribante, A.; Arciola, C.R.; Bertuccio, F.R.; Colombo, M. Ozonized Gel Against Four Candida Species: A Pilot Study and Clinical Perspectives. *Materials* **2020**, *13*, 1731.
23. Park GH, Lee SY, Lee JB, Chang BS, Lee JK, Um HS. Effect of photodynamic therapy according to differences in photosensitizers on Staphylococcus aureus biofilm on titanium. *Photodiagnosis Photodyn Ther.* **2023** Mar; 41:103317.
24. Gallo, S.; Scribante, A. Ozone therapy in dentistry: From traditional applications towards innovative ones. A review of the literature. *IOP Conf. Ser. Earth Environ. Sci.* **2021**, *707*, 012001.
25. Colombo, M.; Gallo, S.; Garofoli, A.; Poggio, C.; Arciola, C.R.; Scribante, A. Ozone Gel in Chronic Periodontal Disease: A Randomized Clinical Trial on the Anti-Inflammatory Effects of Ozone Application. *Biology* **2021**, *10*, 625.
26. Gupta, G.; Mansi, B. Ozone therapy in periodontics. *J. Med. Life* **2012**, *5*, 59–67.
27. Merigo, E.; Rocca, J.P.; Pinheiro, A.L.B.; Fornaini, C. Photobiomodulation Therapy in Oral Medicine: A Guide for the Practitioner with Focus on New Possible Protocols. *Photobiomodul. Photomed. Laser Surg.* **2019**, *37*, 669–680.
28. Sfondrini, M.F.; Vitale, M.; Pinheiro, A.L.B.; Gandini, P.; Sorrentino, L.; Iarussi, U.M.; Scribante, A. Photobiomodulation and Pain Reduction in Patients Requiring Orthodontic Band Application: Randomized Clinical Trial. *Biomed. Res. Int.* **2020**, *2020*, 7460938.
29. Sun, G.; Tunér, J. Low-level laser therapy in dentistry. *Dent. Clin. N. Am.* **2004**, *48*, 1061–1076.

30. Caruso, U.; Nastri, L.; Piccolomini, R.; d'Ercole, S.; Mazza, C.; Guida, L. Use of diode laser 980 nm as adjunctive therapy in the treatment of chronic periodontitis. A randomized controlled clinical trial. *New Microbiol.* **2008**, *31*, 513–518.
31. Saygun, I.; Nizam, N.; Ural, A.U.; Serdar, M.A.; Avcu, F.; Tözüm, T.F. Low-level laser irradiation affects the release of basic fibroblast growth factor (bFGF), insulin-like growth factor-I (IGF-I), and receptor of IGF-I (IGFBP3) from osteoblasts. *Photomed. Laser Surg.* **2012**, *30*, 149–154.
32. Ezber A, Taşdemir İ, Yılmaz HE, Narin F, Sağlam M. Different application procedures of Nd:YAG laser as an adjunct to scaling and root planning in smokers with stage III grade C periodontitis: a single-blind, randomized controlled trial. *Ir J Med Sci*. **2023** Feb;192(1):457-466.
33. Özberk, S.S.; Gündoğar, H.; Özkaya, M.; Taner, İ.L.; Erciyas, K. The effect of photobiomodulation therapy on nonsurgical periodontal treatment in patients with type 2 diabetes mellitus: A randomized controlled, single-blind, split-mouth clinical trial. *Lasers Med. Sci.* **2020**, *35*, 497–504.
34. Karkhanechi, M.; Chow, D.; Sipkin, J.; Sherman, D.; Boylan, R.J.; Norman, R.G.; Craig, R.G.; Cisneros, G.J. Periodontal status of adult patients treated with fixed buccal appliances and removable aligners over one year of active orthodontic therapy. *Angle Orthod.* **2013**, *83*, 146–151.
35. de Oliveira RR, Schwartz-Filho HO, Novaes AB Jr, Taba M Jr. Antimicrobial photodynamic therapy in the non-surgical treatment of aggressive periodontitis: a preliminary randomized controlled clinical study. J Periodontol. 2007 Jun;78(6):965-73.
36. Berglundh, T.; Armitage, G.; Araujo, M.G.; Avila-Ortiz, G.; Blanco, J.; Camargo, P.M.; Chen, S.; Cochran, D.; Derks, J.; Figuero, E.; et al. Peri-implant diseases and conditions: Consensus report of workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J. Clin. Periodontol.* **2018**, *45*, S286–S291.
37. Lesaffre, E.; Philstrom, B.; Needleman, I.; Worthington, H. The design and analysis of split-mouth studies: What statisticians and clinicians should know. *Stat. Med.* **2009**, *28*, 3470–3482.
38. Rapone, B.; Ferrara, E.; Corsalini, M.; Converti, I.; Grassi, F.R.; Santacroce, L.; Topi, S.; Gnoni, A.; Scacco, S.; Scarano, A.; et al. The Effect of Gaseous Ozone Therapy in Conjunction with Periodontal Treatment on Glycated Hemoglobin Level in Subjects with Type 2 Diabetes Mellitus: An Unmasked Randomized Controlled Trial. *Int. J. Environ. Res. Public Health* **2020**, *17*, 5467.
39. Fernandes-Dias, S.B.; de Marco, A.C.; Santamaria, M., Jr.; Kerbauy, W.D.; Jardini, M.A.; Santamaria, M.P. Connective tissue graft associated or not with low laser therapy to treat gingival recession: Randomized clinical trial. *J. Clin. Periodontol.* **2015**, *42*, 54–61.
40. Yılmaz, S.; Algan, S.; Gursoy, H.; Noyan, U.; Kuru, B.E.; Kadir, T. Evaluation of the clinical and antimicrobial effects of the Er:YAG laser or topical gaseous ozone as adjuncts to initial periodontal therapy. *Photomed. Laser Surg.* **2013**, *31*, 293–298.
41. Piepho, H.P. An Algorithm for a Letter-Based Representation of All-Pairwise Comparisons. *J. Comput. Graph. Stat.* **2004**, *13*, 456–466.
42. Scribante, A.; Poggio, C.; Gallo, S.; Riva, P.; Cuocci, A.; Carbone, M.; Arciola, C.R.; Colombo, M. In Vitro Re-Hardening of Bleached Enamel Using Mineralizing Pastes: Toward Preventing Bacterial Colonization. *Materials* **2020**, *13*, 818.
43. Deng, Z.L.; Szafrański, S.P.; Jarek, M.; Bhuju, S.; Wagner-Döbler, I. Dysbiosis in chronic periodontitis: Key microbial players and interactions with the human host. *Sci. Rep.* **2017**, *7*, 3703–3715.
44. Huth, K.C.; Quirling, M.; Lenzke, S.; Paschos, E.; Kamereck, K.; Brand, K.; Hickel, R.; Ilie, N. Effectiveness of ozone against periodontal pathogenic microorganisms. *Eur. J. Oral Sci.* **2011**, *119*, 204–210.
45. Gandhi, K.K.; Cappetta, E.G.; Pavaskar, R. Effectiveness of the adjunctive use of ozone and chlorhexidine in patients with chronic periodontitis. *BDJ Open.* **2019**, *5*, 17.

46. Talmaç, A.C.; Çalişir, M. Efficacy of gaseous ozone in smoking and non-smoking gingivitis patients. *Ir. J. Med. Sci.* **2021**, *190*, 325–333.
47. Convissar, R.; Ross, G. Photobiomodulation Lasers in Dentistry. *Semin. Orthod.* **2020**, *26*, 102–106.
48. Rapone, B.; Ferrara, E.; Santacroce, L.; Topi, S.; Gnoni, A.; Dipalma, G.; Mancini, A.; Di Domenico, M.; Tartaglia, G.M.; Scarano, A.; et al. The Gaseous Ozone Therapy as a Promising Antiseptic Adjuvant of Periodontal Treatment: A Randomized Controlled Clinical Trial. *Int. J. Environ. Res. Public Health* **2022**, *19*, 985.
49. Dompe, C.; Moncrieff, L.; Matys, J.; Grzech-Leśniak, K.; Kocherova, I.; Bryja, A.; Bruska, M.; Dominiak, M.; Mozdziak, P.; Skiba, T.H.I.; et al. Photobiomodulation—Underlying Mechanism and Clinical Applications. *J. Clin. Med.* **2020**, *9*, 1724.
50. Al-Rabiah, M.; Al-Hamoudi, N.; Al-Aali, K.A.; Slapar, L.; AlHelal, A.; Al Deeb, M.; Mokeem, S.A.; Vohra, F.; Abduljabbar, T. Efficacy of Scaling and Root Planing with Photobiomodulation for Treating Periodontitis in Gutka Chewers: A Randomized Controlled Trial. *Photobiomodul. Photomed. Laser Surg.* **2020**, *38*, 545–551.
51. Ren, C.; McGrath, C.; Jin, L.; Zhang, C.; Yang, Y. The effectiveness of low-level laser therapy as an adjunct to non-surgical periodontal treatment: A meta-analysis. *J. Periodontal. Res.* **2017**, *52*, 8–20.
52. Dalvi, S.; Benedicenti, S.; Hanna, R. Effectiveness of Photobiomodulation as an Adjunct to Nonsurgical Periodontal Therapy in the Management of Periodontitis- A Systematic Review of in vivo Human Studies. *Photochem. Photobiol.* **2021**, *97*, 223–242.
53. Cronshaw, M.; Parker, S.; Anagnostaki, E.; Mylona, V.; Lynch, E.; Grootveld, M. Photobiomodulation and Oral Mucositis: A Systematic Review. *Dent. J.* **2020**, *8*, 87.
54. Meimandi, M.; Talebi Ardakani, M.R.; Esmaeil Nejad, A.; Yousefnejad, P.; Saebi, K.; Tayeed, M.H. The Effect of Photodynamic Therapy in the Treatment of Chronic Periodontitis: A Review of Literature. *J. Lasers Med. Sci.* **2017**, *8*, S7–S11.
55. Sechi, L.A.; Lezcano, I.; Nunez, N.; Espim, M.; Duprè, I.; Pinna, A.; Molicotti, P.; Fadda, G.; Zanetti, S. Antibacterial activity of ozonized sunflower oil (Oleozon). *J. Appl. Microbiol.* **2001**, *90*, 279–284.
56. Lezcano, I.; Nuñez, N.; Espino, M.; Gómez, M. Antibacterial activity of ozonized sunflower oil, oleozon, against *Staphylococcus aureus* and *Staphylococcus epidermidis*. *Ozone Sci. Eng.* **2000**, *22*, 207–214.