Artificial Intelligence–Driven Molecular Docking for Selection of Antibacterial Agents in Periodontitis Therapy: From Pathophysiology to Target Validation

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ABSTRACT

Periodontitis is a chronic inflammatory disease that leads to destruction of the supporting structures of teeth and eventually tooth loss. The disease is initiated by pathogenic bacteria and modified by host immune responses. Although mechanical cleaning remains the foundation of therapy, antibiotics are often required in moderate to severe cases. However, empirical drug selection, increasing resistance, and variable patient response limit treatment success. Artificial intelligence (AI) and molecular docking have recently emerged as powerful tools for improving precision in antimicrobial selection. These technologies allow prediction of drug–target interactions, screening of potential molecules, and optimization of therapy before clinical use. This review discusses the pathophysiology of periodontitis, the role of antibiotics such as minocycline and clindamycin, and the growing importance of AI-assisted molecular docking in periodontal drug discovery and validation.

INTRODUCTION

Periodontal disease refers to a group of conditions that affect the periodontium, the supporting structures of the teeth, including the gingiva, alveolar bone, cementum, and periodontal ligament. Early detection and timely management are essential to prevent long-term complications. Gingivitis is the mildest form of periodontal disease, affecting up to 90% of the population. Gingivitis is characterized by inflammation of the gingiva caused by the accumulation of bacteria and debris along the gum line, leading to the formation of dental plaque. This condition is reversible with improved oral hygiene. However, if left untreated, gingivitis can progress to periodontitis.

Periodontitis is a chronic, destructive inflammatory disease affecting the supporting structures of the teeth, predominantly caused by pathogenic bacteria such as Porphyromonas gingivalis, Tannerella forsythia, and Treponema denticola. These organisms produce virulence factors that degrade host tissues and modulate immune responses. The optimal antibiotic used in periodontal diseases should be bactericidal at therapeutic doses, have antimicrobial activity against a variable spectrum of pathogens specific to periodontal infections, should induce a minimal bacterial resistance, have good tissue penetration and be well tolerated.

Molecular docking studies help predict the binding mode and affinity of small molecules (ligands) to protein targets. They play an essential role in structure-based drug design and repurposing of existing drugs for new therapeutic applications, including periodontal therapy.

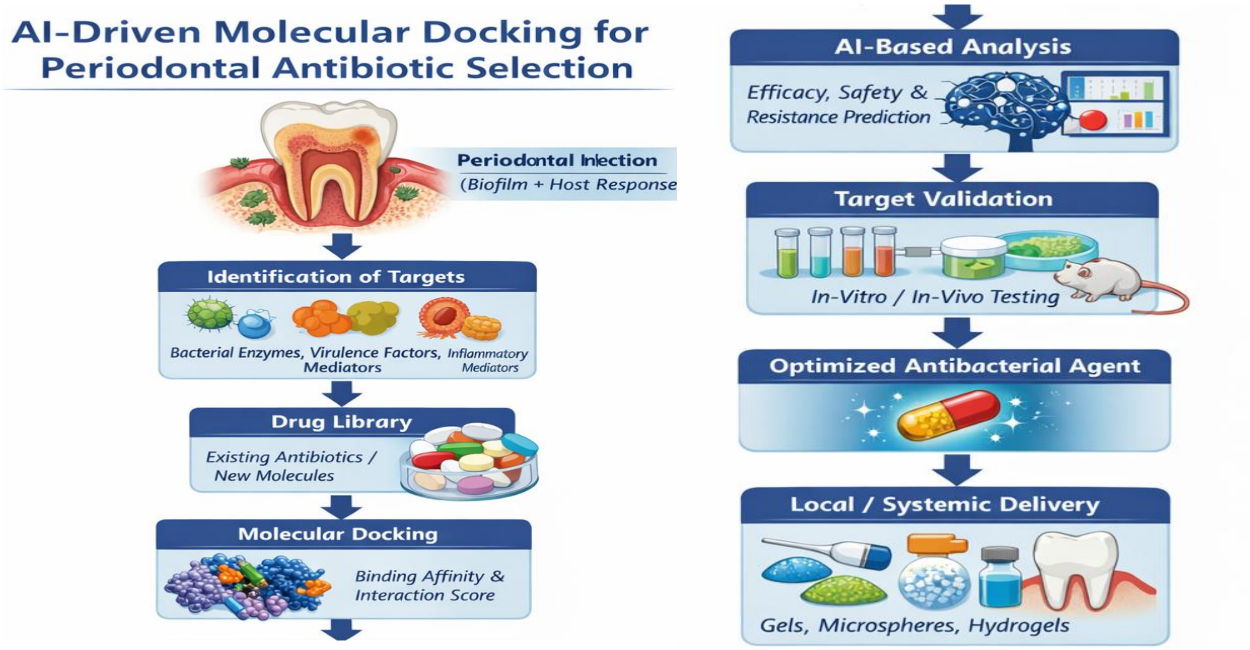

Figure 1: AI-Driven Molecular Docking for Peridontal Antibiotic Selection

Current Treatment of Periodontitis

The current treatment of periodontitis aims to eliminate microbial plaque, reduce periodontal inflammation, halt disease progression, and preserve periodontal support. Management is based on a stepwise approach, combining non-surgical, surgical, and maintenance therapies depending on disease severity and patient response.

1. Non-Surgical Periodontal Therapy

This is the first line of treatment and includes patient education, motivation, and scaling and root planing (SRP) to remove supra- and subgingival plaque and calculus. Effective plaque control by the patient is critical for treatment success.

2. Adjunctive Antimicrobial Therapy

In moderate to severe or refractory cases, local drug delivery systems (e.g., chlorhexidine chips, doxycycline gel) or systemic antibiotics (such as amoxicillin with metronidazole or clindamycin in penicillin-allergic patients) may be used as adjuncts to SRP to control pathogenic bacteria.

3. Surgical Periodontal Therapy

Surgical intervention is indicated when deep periodontal pockets persist after non-surgical therapy. Procedures include flap surgery, resective surgery, and regenerative techniques such as guided tissue regeneration and bone grafting to restore lost periodontal structures.

4. Supportive Periodontal Therapy (Maintenance)

Long-term success depends on regular periodontal maintenance, including professional cleaning, monitoring of periodontal parameters, and reinforcement of oral hygiene practices to prevent disease recurrence.

Despite the availability of diverse treatment modalities, recurrence of disease is common, and outcomes are not always satisfactory. Biofilm resistance, variability in host response, adverse drug reactions, and difficulties in selecting the most effective antimicrobial agent continue to limit success. Consequently, modern research is shifting toward precision approaches, including computational prediction and artificial intelligence tools, to identify optimal drug candidates and improve targeted therapy.

Need for Artificial Intelligence and Molecular Docking in Periodontal Drug Selection

Periodontal diseases are complex, multifactorial inflammatory conditions involving host–microbe interactions, genetic susceptibility, and environmental factors. Conventional drug selection in periodontology is largely empirical and may not account for individual variability in microbial profiles and host responses. Therefore, Artificial Intelligence (AI) and molecular docking have emerged as powerful tools to improve precision and effectiveness in periodontal drug selection.

Role and Need for Artificial Intelligence

Artificial Intelligence enables the analysis of large datasets such as microbial genomics, clinical parameters, radiographic findings, and treatment outcomes. AI algorithms can identify disease patterns, predict treatment response, and assist in selecting the most effective antimicrobial or host-modulatory drug for a specific patient. This supports a personalized and evidence-based approach, reducing trial-and-error prescribing and minimizing antimicrobial resistance.

Role and Need for Molecular Docking

Molecular docking is a computational technique that predicts the binding affinity and interaction between drugs and specific molecular targets such as bacterial enzymes, virulence factors, or host inflammatory mediators. In periodontology, docking helps screen potential drugs against key periodontal pathogens (Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans) and host targets, thereby accelerating drug discovery, repurposing existing drugs, and optimizing drug efficacy.

Combined Impact on Periodontal Drug Selection

The integration of AI with molecular docking allows rapid virtual screening of drug candidates, prediction of therapeutic outcomes, and identification of optimal drug–target combinations. This approach reduces time, cost, and dependence on extensive laboratory testing, leading to more targeted, safer, and effective periodontal therapies.

Applications of Molecular Docking in Drug Discovery and Periodontal Therapeutics

Molecular docking is a computational technique used to predict the interaction between a drug molecule (ligand) and a biological target (protein or enzyme). It plays a vital role in modern drug discovery and has increasing applications in periodontal therapeutics, where targeted antimicrobial and host-modulatory strategies are essential.

Applications in Periodontal Therapeutics

1. Targeting Periodontal Pathogens
   Docking is used to evaluate drug interactions with key periodontal pathogens such as Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans, particularly their virulence factors and enzymes.
2. Development of Targeted Antimicrobials
   It assists in designing antimicrobials that specifically inhibit periodontal pathogens while minimizing effects on the beneficial oral microbiome.
3. Host Modulation Therapy
   Molecular docking helps identify drugs that modulate host inflammatory mediators (e.g., matrix metalloproteinases, cytokines), reducing tissue destruction in periodontitis.
4. Biomaterial and Local Drug Delivery Research
   Docking supports the selection of drugs for incorporation into local delivery systems such as gels, fibers, and nanoparticles used in periodontal pockets.

Comparative Study of Clindamycin and Minocycline in Periodontal Diseases (Review-based Evidence)

Clindamycin and minocycline are both well-established antibiotics used as adjuncts to mechanical periodontal therapy, but they differ in drug class, mode of delivery, biological properties, and clinical indications. Clindamycin, a lincosamide antibiotic, is primarily used as a systemic agent, especially in patients who are allergic to penicillin or in cases of severe, refractory, or aggressive periodontitis. Review literature reports that clindamycin demonstrates strong activity against anaerobic periodontal pathogens, including Porphyromonas gingivalis, Prevotella intermedia, and Fusobacterium nucleatum. Due to its excellent penetration into gingival crevicular fluid, periodontal tissues, and bone, clindamycin has shown clinical improvements in probing depth (PD) reduction and bleeding on probing (BOP) comparable to conventional systemic regimens such as amoxicillin–metronidazole. Reviews and clinical studies indicate mean PD reductions of approximately 1.5–2.5 mm when clindamycin is used as an adjunct to scaling and root planing, particularly in advanced periodontitis cases.

Minocycline, a semisynthetic tetracycline derivative, has been extensively studied in periodontology, predominantly as a local drug delivery agent (microspheres or gels), although systemic use has also been reported. Review papers consistently show that locally delivered minocycline provides significant additional benefits over scaling and root planing alone. These benefits include reductions in probing depth of approximately 1.0–2.0 mm and gains in clinical attachment level (CAL), particularly in deep periodontal pockets (≥5 mm). In addition to its antimicrobial action, minocycline exhibits host-modulatory properties, such as inhibition of matrix metalloproteinases and suppression of collagen breakdown, which contribute to reduced periodontal tissue destruction. Because of its local application, minocycline achieves high subgingival concentrations with minimal systemic exposure, making it especially suitable for localized and persistent periodontal pockets.

Comparative evidence from review literature suggests that while both drugs are effective, their clinical roles differ. Clindamycin is favored in generalized, severe, or systemic conditions associated with periodontitis, whereas minocycline is preferred for site-specific therapy and long-term periodontal maintenance. Clindamycin use is limited by the risk of gastrointestinal adverse effects, including Clostridioides difficile–associated colitis, whereas minocycline is generally well tolerated when used locally. Overall, reviews conclude that minocycline has stronger evidence and wider acceptance in routine periodontal therapy due to its safety and localized delivery, while clindamycin remains an important alternative systemic antibiotic in selected clinical situations.

DISCUSSION & FUTURE PERSPECTIVES

Artificial intelligence–driven molecular docking provides a structured pathway for identifying effective antibacterial therapies in periodontitis. The process begins with understanding periodontal infection, where microbial biofilms interact with the host immune system and initiate tissue destruction. Key bacterial enzymes, virulence factors, and inflammatory mediators are then selected as therapeutic targets. A library of existing antibiotics or novel molecules is screened computationally. Molecular docking predicts how strongly each drug binds to the chosen target and estimates interaction stability. These results are further refined using AI-based analytics, which rank candidates according to predicted efficacy, safety, and likelihood of resistance. Promising agents proceed to experimental validation through in-vitro and in-vivo studies. Once confirmed, optimized drugs can be incorporated into appropriate delivery platforms such as gels, microspheres, or hydrogels for localized or systemic administration. This integrated digital approach accelerates discovery, improves accuracy, and supports the development of personalized periodontal treatment strategies.

CONCLUSION

Artificial intelligence and molecular docking enhance periodontal therapy by enabling precise antibiotic selection, improving target validation, reducing resistance, and supporting development of safer, personalized local treatments.

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