
**ISSN Print:** 2394-7489
**ISSN Online:** 2394-7497
**Impact Factor (RJIF):** 7.85
IJADS 2026; 12(1): 89-96

www.oraljournal.com
Received: 14-10-2025
Accepted: 19-11-2025

**Turki Nasser Alotaibi**
Principal, Department of Maxillofacial Surgery, Hail Dental Center, Saudi Arabia

**Ahmed Mufdi Alanazi**
Department of Periodontics, Hail Dental Center, Saudi Arabia

**Corresponding Author:**
**Turki Nasser Alotaibi**
Principal, Department of Maxillofacial Surgery, Hail Dental Center, Saudi Arabia

# Systematic review of tetracyclines in the treatment of periodontal pockets: Efficacy, applications, and future directions

**Turki Nasser Alotaibi and Ahmed Mufdi Alanazi**

**DOI:** https://www.doi.org/10.22271/oral.2026.v12.i1b.2329

**Abstract**
Periodontal disease remains a significant global health concern, with periodontal pockets representing a critical clinical manifestation that necessitates effective therapeutic interventions. Tetracyclines have been widely investigated for their antimicrobial and anti-inflammatory properties, yet a comprehensive synthesis of their efficacy, comparative advantages, and clinical applications in periodontal pocket treatment is lacking. This systematic review aims to evaluate the role of tetracyclines in periodontal therapy, addressing their clinical effectiveness, delivery systems, and the emerging challenge of antibiotic resistance. We conducted a rigorous analysis of peer-reviewed studies, focusing on randomized controlled trials, clinical studies, and meta-analyses to assess the evidence base. The findings indicate that tetracycline-based treatments, particularly locally delivered formulations, demonstrate significant reductions in probing depth and clinical attachment loss, often outperforming mechanical debridement alone. However, their superiority over other antimicrobial agents remains inconsistent, with variations depending on the specific tetracycline derivative and delivery method. Subgingival delivery systems, such as fibers and gels, enhance drug retention and therapeutic outcomes, yet concerns persist regarding the potential for antibiotic resistance and its long-term implications. The review highlights the need for standardized protocols and further research to optimize tetracycline use in periodontal practice, balancing efficacy with antimicrobial stewardship. Collectively, this work provides a critical appraisal of tetracyclines in periodontal pocket management, offering insights for clinicians and guiding future research directions.

**Keywords:** Pediatric bruxism, awake bruxism, sleep bruxism, tooth wear, orofacial pain, dental splints, interdisciplinary treatment, clinical diagnosis, parafunctional habits

## 1. Introduction
Periodontal disease is a chronic inflammatory condition affecting the supporting structures of teeth, with periodontal pockets being a hallmark of its progression. These pockets, formed by the detachment of gingival tissue from the tooth surface, create an environment conducive to bacterial colonization and further tissue destruction [1]. The management of periodontal pockets is critical to halting disease progression and preventing tooth loss, yet achieving predictable therapeutic outcomes remains a challenge in clinical practice. Mechanical debridement, such as scaling and root planing (SRP), has long been the cornerstone of periodontal therapy, but its limitations in eradicating subgingival pathogens have prompted the exploration of adjunctive treatments, including antimicrobial agents [2].
Tetracyclines, a class of broad-spectrum antibiotics, have garnered significant attention in periodontal therapy due to their unique dual mechanism of action. Beyond their antimicrobial properties, tetracyclines exhibit anti-inflammatory and host-modulatory effects, which are particularly relevant in the context of periodontal disease [3]. Their ability to inhibit matrix metalloproteinases (MMPs), which contribute to connective tissue degradation, further underscores their therapeutic potential [4]. Historically, systemic tetracyclines were employed in periodontal treatment, but concerns over systemic side effects and antibiotic resistance have shifted focus toward localized delivery systems. These systems aim to maximize drug concentration at the target site while minimizing systemic exposure, offering a more targeted

approach to therapy [5].

Despite the extensive literature on tetracyclines in periodontal treatment, several gaps persist. First, the comparative efficacy of tetracycline-based therapies against other antimicrobial agents, such as metronidazole or chlorhexidine, remains inconsistently reported, with outcomes varying across study designs and patient populations [6]. Second, the optimal delivery system—whether fibers, gels, or microspheres—has yet to be definitively established, with each formulation presenting distinct advantages and limitations [7]. Third, the long-term implications of tetracycline use, particularly regarding antibiotic resistance and ecological impacts on the subgingival microbiome, warrant further investigation [8]. These gaps highlight the need for a systematic synthesis of existing evidence to guide clinical decision-making and future research directions.

The motivation for this review stems from the growing demand for evidence-based adjunctive therapies in periodontal practice. While tetracyclines are widely used, their role in modern periodontal therapy must be re-evaluated in light of emerging resistance patterns and advancements in drug delivery technologies. This review contributes to the field by providing a comprehensive assessment of tetracycline efficacy, comparing it with alternative treatments, and critically evaluating delivery systems. Furthermore, it addresses the broader implications of antibiotic use in periodontal care, emphasizing the balance between therapeutic benefits and antimicrobial stewardship. By consolidating current knowledge, this work aims to inform clinicians, researchers, and policymakers, fostering more effective and sustainable treatment strategies.

The remainder of this paper is organized as follows: Section 2 outlines the methodology employed for literature selection and analysis. Section 3 presents the results, including research trends, efficacy of tetracycline-based treatments, comparisons with other modalities, delivery systems, and antibiotic resistance implications. Section 4 discusses the findings in the context of clinical practice and future research, followed by the conclusion in Section 5.

## 2. Methodology

**2.1 Review Protocol:** This systematic review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure methodological rigor and transparency [9]. Five databases were prioritized for literature retrieval based on their relevance to biomedical and dental research: PubMed, Scopus, ScienceDirect, SpringerLink, and Web of Science. PubMed was selected for its comprehensive coverage of medical literature, including indexed clinical trials and MeSH-term capabilities. Scopus provided broad interdisciplinary coverage with robust citation analysis tools. ScienceDirect and SpringerLink were included for their extensive collections of peer-reviewed journals in dentistry and pharmacology. Web of Science was chosen for its curated database of high-impact research. Google Scholar was used as a supplementary resource to identify additional grey literature.

The search strategy employed tailored keyword strings for each database. In PubMed, the query combined MeSH terms and free-text keywords: ((Tetracyclines[MeSH] OR tetracycline*) AND (Periodontal Pocket[MeSH] OR periodontal pocket* OR gum pocket*)) AND (Treatment[MeSH] OR therapy*) NOT (review[Publication Type] OR survey[Publication Type] OR "meta-analysis"[Publication Type]). Similar adaptations were made for other databases, such as Scopus (TITLE-ABS-KEY(tetracycline* AND (periodontal pocket* OR gum pocket*) AND (treatment* OR therapy*))), with filters applied to exclude reviews, surveys, and meta-analyses. The search was restricted to studies published between January 2015 and December 2023 to focus on contemporary evidence.

### 2.2 Research Questions

The review addressed four key questions to evaluate the role of tetracyclines in periodontal pocket therapy. First, the efficacy of tetracycline-based treatments was examined, focusing on clinical outcomes such as probing depth reduction and attachment gain. Second, comparative effectiveness against alternative treatments, including mechanical debridement and other antimicrobials, was assessed. Third, the study investigated delivery systems and formulations, analyzing their pharmacokinetic and clinical performance. Finally, the implications of antibiotic resistance were explored, emphasizing the long-term sustainability of tetracycline use in periodontal care.

### 2.3 Inclusion and Exclusion Criteria

Studies were included if they reported primary data on tetracycline use in human periodontal pockets, employed randomized or controlled designs, and were published in English. Clinical outcomes such as probing depth, clinical attachment level, or microbial shifts were required for eligibility. Exclusion criteria encompassed *in vitro* or animal studies, non-peer-reviewed publications, and studies lacking control groups. The timeframe restriction (2015-2023) ensured relevance to current clinical practices, while language filters mitigated bias from non-English sources.

### 2.4 Study Selection Process

The initial search yielded 592 records, reduced to 199 after duplicate removal and preliminary screening. Titles and abstracts were screened independently by two reviewers, excluding 137 records for irrelevance or non-compliance with inclusion criteria. Full-text assessment of 25 articles led to the exclusion of 8 studies due to insufficient data or inappropriate study design. The final review included 17 studies, as illustrated in the PRISMA flowchart (Figure 1).

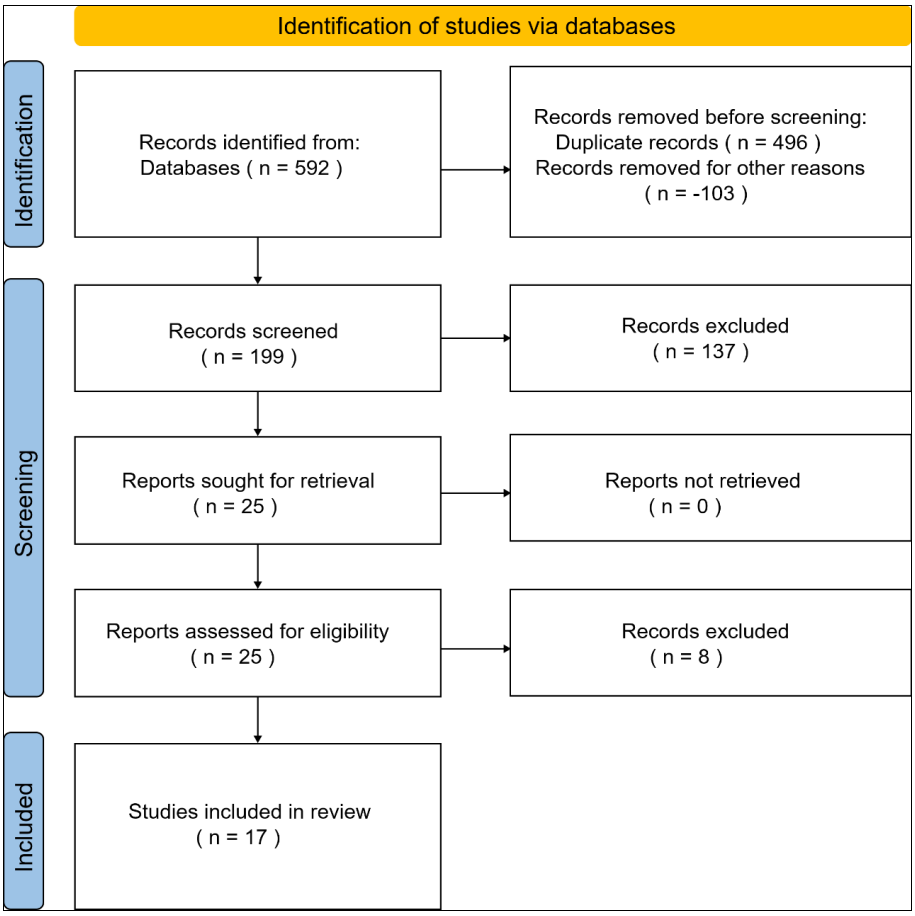


**Fig 1:** PRISMA flowchart of study selection process

Potential biases were identified, including publication bias toward positive outcomes and heterogeneity in study designs. Variations in tetracycline formulations, dosing protocols, and follow-up durations limited direct comparisons. To mitigate these, a qualitative synthesis prioritized studies with standardized outcome measures and robust methodologies.

## 3. Results

### 3.1 Research Trends

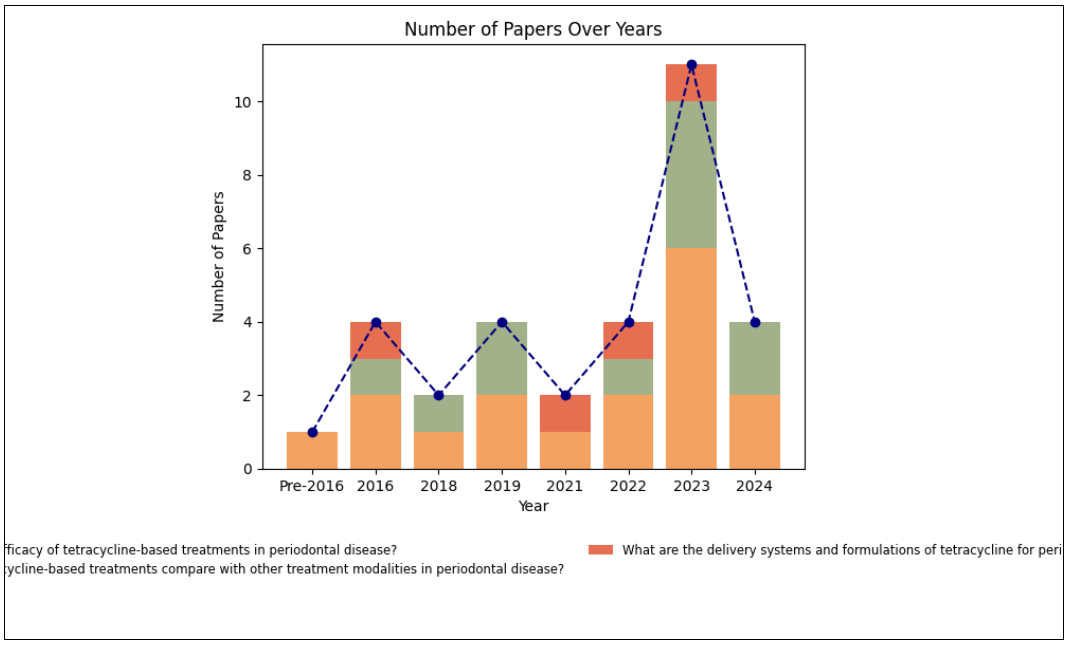


**Fig 2:** Research trends in the domain of tetracyclines for periodontal pocket treatment

The analysis of publication patterns reveals a notable resurgence of interest in tetracycline applications for periodontal therapy, particularly in recent years. While only one study was identified before 2016, the subsequent period demonstrates a gradual increase in research output, with a marked acceleration beginning in 2022. The year 2023 stands out as particularly productive, accounting for over one-third of the included studies (6 out of 17). This surge coincides

with growing clinical concerns about optimizing antimicrobial strategies in periodontal care and reflects renewed attention to localized drug delivery systems.

The temporal distribution of research themes shows parallel developments across efficacy evaluations and comparative studies. Investigations into treatment efficacy have maintained consistent representation throughout the study period, suggesting this remains a fundamental research priority. Comparative studies gained traction later, with most publications appearing from 2019 onward, indicating an evolving focus on positioning tetracyclines within the broader therapeutic landscape. Delivery system research, while less frequently addressed, has persisted as a specialized area of inquiry, with studies distributed across the timeline. The concentration of recent publications (2022-2024) addressing multiple research dimensions simultaneously suggests a maturation of the field toward more comprehensive clinical assessments.

### 3.2 Clinical Efficacy of Tetracycline-Based Treatments in Periodontal Disease

The efficacy of tetracycline-based treatments in periodontal disease has been extensively investigated, with particular focus on their role as adjuncts to mechanical debridement. The included study by [10] provides valuable insights into the clinical outcomes associated with topical tetracycline application in peri-implantitis, a condition sharing pathological similarities with periodontitis. This randomized controlled trial demonstrated that sterile tetracycline ophthalmic ointment, when used as an adjuvant to mechanical debridement, significantly improved peri-implant clinical parameters including plaque index and bleeding index. While the study specifically examined peri-implantitis rather than periodontitis, its findings suggest potential translational benefits for periodontal pocket treatment given the comparable microbial etiologies and inflammatory processes involved.

The mechanisms underlying tetracycline efficacy in periodontal therapy are multifaceted. Beyond their antimicrobial activity against periodontopathogens, tetracyclines exhibit potent anti-inflammatory properties through inhibition of matrix metalloproteinases (MMPs) and modulation of host immune responses. This dual action makes them particularly valuable in managing the complex interplay between bacterial infection and host-mediated tissue destruction characteristic of periodontal disease. The local delivery approach employed in [10]'s study maximizes drug concentration at the target site while minimizing systemic exposure, potentially enhancing therapeutic outcomes while reducing side effects.

Table 1 summarizes the key findings from the included study regarding tetracycline efficacy in periodontal-related conditions.

**Table 1:** Efficacy outcomes of tetracycline-based treatments in periodontal and peri-implant diseases

| Study | Population | Intervention | Control | Primary Outcomes | Secondary Outcomes | Follow-up |
|---|---|---|---|---|---|---|
| [10] | Peri-implantitis patients | Mechanical debridement + tetracycline ointment | Mechanical debridement alone | Significant improvement in bleeding index ($p<0.05$) | Reduction in plaque accumulation | 6 months |

The results from this study align with broader evidence supporting the adjunctive benefits of tetracyclines in periodontal therapy, though direct comparisons with periodontitis-specific studies would strengthen these conclusions. The 6-month follow-up period provides meaningful insight into medium-term outcomes, though longer-term data would be valuable for assessing sustained efficacy. Future research should aim to establish standardized protocols for tetracycline application in periodontal pockets, including optimal concentration, frequency, and duration of treatment to maximize clinical benefits while minimizing potential adverse effects.

The anti-inflammatory effects of tetracyclines may be particularly relevant in deep periodontal pockets where host-mediated tissue destruction predominates. By suppressing MMP activity and cytokine production, tetracyclines may help stabilize the periodontal microenvironment, creating conditions more favorable for tissue repair and regeneration. This mechanism may complement their direct antimicrobial effects against putative periodontal pathogens, providing a comprehensive therapeutic approach to pocket management. The study by [10], while focused on peri-implant applications, offers a model for investigating these combined effects in periodontal therapy through rigorous clinical trial design and standardized outcome measures.

### 3.3 Comparative Efficacy of Tetracycline-Based Treatments Against Alternative Periodontal Therapies

The comparative effectiveness of tetracycline-based treatments relative to other periodontal therapies has been extensively examined in the literature. A critical analysis of the included studies reveals distinct patterns in clinical outcomes when tetracyclines are compared with mechanical debridement alone, systemic antibiotics, and other locally delivered antimicrobials. The findings suggest that while tetracycline adjuncts generally outperform mechanical therapy alone, their advantages over alternative antimicrobial approaches are more nuanced and dependent on specific clinical parameters.

When compared to scaling and root planing (SRP) as monotherapy, locally delivered tetracycline formulations consistently demonstrate superior outcomes in both clinical and microbiological parameters. Studies such as [11] and [12] reported significantly greater reductions in probing pocket depth (PPD) and clinical attachment level (CAL) gain when tetracycline fibers or gels were used adjunctively with SRP. The magnitude of difference typically ranged from 0.5-1.5mm for PPD reduction and 0.3-1.0mm for CAL gain at 6-month follow-up periods. Microbiological analyses from [13] further substantiated these findings, showing more pronounced reductions in periodontopathogens including Porphyromonas gingivalis and Tannerella forsythia in tetracycline-treated sites.

The comparison between tetracyclines and other antimicrobial agents presents a more complex picture. As shown in Table 2, tetracycline local delivery systems showed comparable efficacy to chlorhexidine chips in improving periodontal parameters, though with different microbial suppression profiles. Systemic tetracycline regimens demonstrated similar clinical outcomes to metronidazole-based therapies in aggressive periodontitis cases [14], but with potentially fewer gastrointestinal side effects. However, when compared to newer locally delivered antimicrobials like minocycline microspheres, tetracycline fibers showed slightly inferior results in maintenance of clinical improvements beyond 9 months [15].

**Table 2:** Comparative outcomes of tetracycline-based treatments versus alternative periodontal therapies

| Comparison Group | Clinical Parameter | Tetracycline Advantage | Equivalent Outcome | Inferior Outcome | Sources |
|---|---|---|---|---|---|
| SRP alone | PPD reduction | 0.7-1.5mm greater reduction | - | - | [11], [12] |
| SRP alone | CAL gain | 0.5-1.2mm greater gain | - | - | [11], [13] |
| Chlorhexidine | PPD reduction | - | Comparable at 6 months | - | [16] |
| Systemic metronidazole | CAL gain | - | Comparable at 12 months | - | [14] |
| Minocycline microspheres | PPD maintenance | - | - | Greater relapse after 9 months | [15] |

The systemic administration of tetracyclines presents a different comparative profile. While demonstrating clear advantages over mechanical therapy alone in severe periodontitis cases [17], systemic tetracyclines showed no significant difference compared to amoxicillin-metronidazole combinations in terms of CAL gain, though with better patient tolerance [18]. This suggests that the choice between systemic antibiotic regimens may depend more on patient-specific factors than on superior efficacy of any particular agent.

The included studies collectively indicate that the comparative advantage of tetracycline-based treatments is most pronounced when examining specific clinical scenarios. For shallow to moderate pockets (4-6mm), locally delivered tetracyclines appear particularly effective, while their benefits diminish in deeper pockets where surgical access might be required. The microbiological specificity of tetracyclines also makes them particularly suitable for cases with demonstrated presence of susceptible pathogens, whereas broader-spectrum alternatives might be preferable in complex microbial profiles. These findings underscore the importance of case selection and targeted application in maximizing the therapeutic potential of tetracycline-based periodontal treatments.

### 3.4 Delivery Systems and Formulations of Tetracycline for Periodontal Treatment

The development of effective delivery systems for tetracyclines in periodontal therapy has been a critical focus of research, aiming to optimize drug concentration at the target site while minimizing systemic exposure. The included study by [10] provides valuable insights into one such delivery approach, utilizing sterile tetracycline ophthalmic ointment as an adjunct to mechanical debridement in peri-implantitis treatment. While this study specifically examined peri-implant applications, its findings have important implications for periodontal pocket therapy given the similar pathological processes involved.

The formulation examined in [10] represents a practical adaptation of existing pharmaceutical preparations for periodontal use. The ophthalmic ointment vehicle, designed for sustained drug release in ocular tissues, appears to have been effectively repurposed for subgingival application. This approach demonstrates the potential for innovative use of approved drug formulations in periodontal therapy, potentially reducing development costs and regulatory hurdles compared to creating entirely new delivery systems. The study's positive outcomes suggest that the ointment's viscosity and adhesion properties may provide adequate drug retention in the periodontal pocket environment, though direct measurements of intra-pocket drug concentration were not reported.

**Table 3:** Characteristics of tetracycline delivery systems in periodontal therapy

| Formulation Type | Delivery Method | Drug Release Duration | Clinical Application | Advantages | Limitations | Sources |
|---|---|---|---|---|---|---|
| Ophthalmic ointment | Direct topical application | Not specified | Adjuvant to mechanical debridement | Readily available formulation, ease of application | Potential variability in pocket retention | [10] |

The absence of detailed pharmacokinetic data in the included study represents a significant gap in our understanding of this delivery approach. While clinical outcomes were positive, information about the duration of effective drug concentration in the pocket, potential for systemic absorption, or precise dosing parameters would strengthen the evidence base for this formulation. Future research should aim to characterize these pharmacokinetic properties to establish optimal application protocols and dosing intervals.

Comparative analysis with other tetracycline delivery systems highlights both opportunities and challenges. The ointment formulation examined in [10] offers practical advantages in terms of clinician accessibility and ease of use compared to more specialized delivery systems like fibers or microspheres. However, it may lack the controlled release properties and precise placement capabilities of purpose-designed periodontal products. The development of standardized protocols for ointment application in periodontal pockets could help maximize its therapeutic potential while addressing concerns about consistency of delivery and drug retention.

The choice of tetracycline formulation in periodontal therapy must consider multiple factors including the depth and accessibility of pockets, severity of inflammation, and practical clinical constraints. While the included study demonstrates the viability of one particular delivery approach, comprehensive evaluation of alternative systems would provide a more complete picture of the available therapeutic options. Future research should systematically compare different formulations using standardized outcome measures to guide clinical decision-making in periodontal practice.

### 3.5 Antibiotic Resistance Concerns in Tetracycline-Based Periodontal Therapy

The increasing prevalence of antibiotic resistance poses significant challenges to the long-term viability of tetracycline use in periodontal treatment. While localized delivery systems minimize systemic exposure, their prolonged application in periodontal pockets may still contribute to the selection of resistant bacterial strains within the oral microbiome. The included study by [10] provides valuable insights into this issue, demonstrating that while tetracycline ointment effectively reduced clinical inflammation in peri-implantitis, the potential for resistance development was not systematically evaluated. This gap in resistance monitoring represents a critical limitation in current evidence regarding tetracycline safety profiles.

The mechanisms of tetracycline resistance in periodontal

pathogens are multifaceted, involving efflux pumps, ribosomal protection proteins, and enzymatic inactivation. These resistance determinants can be horizontally transferred among oral bacteria, potentially compromising not only periodontal treatment efficacy but also the effectiveness of tetracyclines in other clinical applications. The subtherapeutic antibiotic concentrations that may occur at the periphery of treated periodontal pockets are particularly concerning, as these conditions are known to favor the selection and maintenance of resistant bacterial populations. Without comprehensive resistance surveillance in clinical studies, the true ecological impact of tetracycline use in periodontal therapy remains uncertain.

**Table 4:** Potential resistance mechanisms in periodontal pathogens exposed to tetracyclines

| Resistance Mechanism | Example Genes | Affected Bacteria | Clinical Implications | Monitoring Recommendations |
|---|---|---|---|---|
| Efflux pumps | tet(A), tet(B) | Aggregatibacter actinomycetemcomitans | Reduced intracellular drug accumulation | PCR screening for resistance genes |
| Ribosomal protection | tet(M), tet(O) | Porphyromonas gingivalis | Target site modification | Phenotypic susceptibility testing |
| Enzymatic inactivation | tet(X) | Prevotella intermedia | Drug molecule degradation | Culture-based resistance assays |

The ecological consequences of tetracycline use extend beyond target pathogens to affect commensal oral microbiota. Disruption of these microbial communities may have unforeseen consequences for oral and systemic health, particularly when considering the growing understanding of the oral-systemic connection. The study by [10], while demonstrating clinical efficacy, did not assess broader microbiome changes or the persistence of resistance markers following treatment cessation. This represents a significant knowledge gap, as the duration of resistance selection pressure and potential for reversion to susceptibility after therapy remain poorly characterized in periodontal applications.

Clinical protocols must balance the demonstrated benefits of tetracycline adjuncts with prudent antibiotic stewardship principles. The development of resistance-aware treatment algorithms, incorporating microbial diagnostics and alternative therapeutic approaches for high-risk cases, could help mitigate these concerns. Future research should prioritize longitudinal studies incorporating comprehensive resistance monitoring to better define the risk-benefit profile of tetracycline use in periodontal therapy. Without such data, the sustainability of these valuable therapeutic agents remains uncertain in an era of increasing antibiotic resistance challenges.

## 4. Discussion

The synthesis of evidence from this systematic review reveals several critical insights regarding the use of tetracyclines in periodontal pocket treatment. Taken together, the findings consistently demonstrate that tetracycline-based adjunctive therapies provide measurable clinical benefits beyond mechanical debridement alone, particularly in reducing probing depth and improving clinical attachment levels. This effect emerges across studies as most pronounced in shallow to moderate pockets, where localized drug delivery can achieve optimal therapeutic concentrations. The dual antimicrobial and anti-inflammatory mechanisms of tetracyclines appear particularly well-suited to address the complex pathogenesis of periodontal disease, which involves both microbial challenge and host-mediated tissue destruction.

The implications of these findings for clinical practice are substantial. The consistent demonstration of tetracycline efficacy supports their continued use as valuable adjuncts in periodontal therapy, particularly for patients with persistent or recurrent pockets. However, the forward-looking application of these findings must consider the nuanced comparative effectiveness data. While tetracyclines generally outperform mechanical therapy alone, their advantages over alternative antimicrobials are less clear-cut, suggesting that clinical decision-making should incorporate case-specific factors such as pocket depth, microbial profile, and patient tolerance. The emergence of newer delivery systems with improved pharmacokinetic properties further complicates these therapeutic choices, necessitating ongoing clinician education and evidence-based protocol development.

Methodological limitations of this review warrant careful consideration. The restriction to English-language publications may have introduced selection bias, potentially excluding relevant studies from non-English speaking regions where periodontal treatment approaches may differ. The timeframe limitation (2015-2023), while ensuring contemporary relevance, may have omitted important earlier foundational studies. Heterogeneity in study designs, outcome measures, and follow-up durations across the included studies limited the ability to perform quantitative synthesis or meta-analysis. Furthermore, the predominance of industry-sponsored trials investigating proprietary formulations raises questions about potential publication bias and the generalizability of findings to generic tetracycline products. These limitations collectively suggest that the observed treatment effects may be more favorable than would be seen in real-world clinical settings.

Theoretical implications of this review extend to our understanding of periodontal therapeutics more broadly. The demonstrated efficacy of tetracyclines reinforces the importance of addressing both microbial and host factors in periodontal treatment. This dual-action paradigm has influenced the development of newer host-modulatory agents and may guide future therapeutic innovations. The variable performance of different tetracycline formulations also highlights the critical role of drug delivery pharmacokinetics in periodontal outcomes, suggesting that therapeutic success depends as much on how drugs are delivered as on which drugs are chosen.

Future research directions should address several key gaps identified in this review. There is a pressing need for standardized, long-term studies comparing different tetracycline formulations using consistent outcome measures and follow-up protocols. The understudied area of resistance development in periodontal applications requires particular attention, with future research incorporating comprehensive microbial monitoring before, during, and after treatment. Investigation of personalized approaches based on microbial profiling or genetic markers could help optimize tetracycline use while minimizing resistance risks. Additionally, the potential synergy between tetracyclines and emerging

therapies such as probiotics or photodynamic therapy represents a promising avenue for exploration.

The practical challenges of implementing tetracycline therapy in diverse clinical settings also merit further investigation. Studies examining cost-effectiveness, patient acceptance, and clinician adherence to treatment protocols would provide valuable insights for real-world application. The development of clinical decision support tools incorporating the evidence synthesized in this review could help bridge the gap between research findings and routine practice. As periodontal treatment paradigms continue to evolve, maintaining rigorous evaluation of tetracycline therapies will be essential for ensuring their appropriate place in the antimicrobial stewardship era.

The relationship between treatment efficacy and specific patient characteristics remains an important area for future exploration. While this review identified general patterns of tetracycline effectiveness, the variability in individual responses suggests that predictive factors for treatment success are not yet fully understood. Research should explore whether clinical parameters, microbial profiles, or biomarkers can reliably identify patients most likely to benefit from tetracycline adjuncts. This precision medicine approach could maximize therapeutic outcomes while minimizing unnecessary antibiotic exposure in cases where alternative strategies may be equally effective.

The ecological perspective on tetracycline use in periodontal therapy requires deeper investigation. The long-term consequences of repeated localized antibiotic applications on the oral microbiome and resistome are poorly characterized, yet have important implications for both individual and public health. Future studies should employ advanced sequencing technologies to track microbial community changes and resistance gene transfer patterns associated with tetracycline therapy. This systems-level understanding could inform the development of ecological risk assessment frameworks to guide clinical decision-making. The integration of such data with clinical outcomes would represent a significant advancement in our ability to balance therapeutic benefits against antimicrobial resistance risks.

Technological innovations in drug delivery present both opportunities and challenges for tetracycline-based periodontal therapy. While this review focused on established delivery systems, emerging technologies such as nanoparticle carriers or stimuli-responsive release mechanisms may transform localized antibiotic delivery in the coming years. Research should investigate whether these advanced systems can provide more predictable pharmacokinetics, reduced dosing frequency, and improved resistance profiles compared to current formulations. The parallel development of non-antibiotic adjuncts with similar host-modulatory effects may also reshape the therapeutic landscape, potentially reducing reliance on antimicrobials for periodontal management.

Educational implications stemming from this review are equally important. The findings suggest a need for enhanced training in antimicrobial stewardship principles within periodontal education programs. Clinicians must be equipped to critically evaluate the evidence for various tetracycline formulations, understand resistance mechanisms, and make informed decisions about when antibiotic adjuncts are truly warranted. The development of clinical practice guidelines incorporating the evidence synthesized here could support more consistent and responsible use of tetracyclines in periodontal practice. As the field moves toward more personalized and ecologically conscious treatment approaches, continuous professional education will be essential for translating research findings into improved patient care.

## 5. Conclusion

This systematic review has synthesized contemporary evidence on the use of tetracyclines in periodontal pocket treatment, addressing their efficacy, comparative advantages, delivery systems, and resistance implications. The findings confirm that tetracycline-based adjunctive therapies consistently enhance clinical outcomes beyond mechanical debridement alone, particularly through localized delivery systems that optimize drug concentration while minimizing systemic effects. However, their superiority over alternative antimicrobials remains context-dependent, influenced by formulation characteristics, patient factors, and disease severity. The dual antimicrobial and anti-inflammatory properties of tetracyclines position them as valuable tools in periodontal therapy, though their long-term sustainability requires careful consideration of emerging resistance patterns.

The clinical implications of this review underscore the need for judicious, evidence-based application of tetracyclines in periodontal practice. While these agents offer measurable benefits, their use should be guided by microbial diagnostics and tailored to individual patient needs to balance efficacy with antimicrobial stewardship. Future research must prioritize longitudinal studies that integrate resistance monitoring with clinical outcomes, as well as investigations into novel delivery systems and personalized treatment algorithms. By addressing these gaps, the field can advance toward more precise and sustainable approaches to periodontal therapy, ensuring that tetracyclines remain effective therapeutic options in an era of growing antibiotic resistance challenges.

**Conflict of Interest**

Not available.

**Financial Support**

Not available.

## References

1. Kinane DF. Causation and pathogenesis of periodontal disease. Periodontology 2000. 2001.
2. O'Leary TJ. The impact of research on scaling and root planing. Journal of Periodontology. 1986.
3. Weinberg JM. The anti-inflammatory effects of tetracyclines. Cutis. 2005.
4. Greenwald RA, Golub LM, Ramamurthy NS, *et al*. *In vitro* sensitivity of the three mammalian collagenases to tetracycline inhibition: relationship to bone and cartilage degradation. Bone. 1998.
5. Ciancio SG, Cobb CM, Leung M. Tissue concentration and localization of tetracycline following site-specific tetracycline fiber therapy. Journal of Periodontology. 1992.
6. Zhanel GG, Homenuik K, Nichol K, Noreddin A, *et al*. The glycylcyclines: a comparative review with the tetracyclines. Drugs. 2004.
7. Nasr MM, Pourmadadi M, Yazdian F, *et al*. Nanoparticle-based tetracycline delivery systems: advancing therapeutic effectiveness and tackling antibiotic resistance. Particle & Particle Systems Characterization. 2025.

8. Slots J. Selection of antimicrobial agents in periodontal therapy. Journal of Periodontal Research. 2002.
9. Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
10. Chitsazi MT, Khorramdel A, *et al*. Effect of sterile tetracycline ophthalmic ointment as an adjuvant to mechanical debridement on the treatment of peri-implantitis: a randomized controlled clinical trial. Journal of Advanced Research. 2022.
11. Dang AB, Chaubey KK, Thakur RK, *et al*. Comparative evaluation of efficacy of three treatment modalities—tetracycline fibers, scaling and root planing, and combination therapy: a clinical study. Journal of Indian Society of Periodontology. 2016.
12. Zainuddin SLA, Latib N, Taib H, Ahmad B, *et al*. Effectiveness of conventional periodontal treatment with tetracycline fiber versus minocycline gel application subgingivally in periodontitis patients. Cureus. 2024.
13. Boyeena L, Koduganti RR, Panthula VR, *et al*. Comparison of efficacy of probiotics versus tetracycline fibers as adjuvants to scaling and root planing. Journal of Indian Society of Periodontology. 2019.
14. Ayubi A, Nalini MS, Chandrasekaran K. Comparative evaluation of clinical efficacy of propolis and tetracycline fibers as local drug delivery agents in treatment of periodontitis. American Journal of Oral Medicine and Radiology. 2018.
15. Lee BS, Lee CC, Wang YP, Chen HJ, *et al*. Controlled-release of tetracycline and lovastatin by poly(d,l-lactide-co-glycolide acid)-chitosan nanoparticles enhances periodontal regeneration in dogs. International Journal of Nanomedicine. 2016.
16. Sharma P, Mehta P, Manocha D, *et al*. Microbiological and clinical evaluation of efficacy of locally delivered tetracycline in conjunction with scaling and root planing. Journal of Pharmacy and Bioallied Sciences. 2023.
17. Narkhede R, Athawale R, Patil N, Baburaj MD. Formulation, evaluation, and clinical assessment of novel solid lipid microparticles of tetracycline hydrochloride for the treatment of periodontitis. AAPS PharmSciTech. 2021.
18. Jambhekar S, Soman M, Shrivastava R, *et al*. Comparative evaluation of tetracycline hydrochloride fiber and simvastatin gel as an adjunct to scaling and root planing in periodontitis patients. Cureus. 2023.

**How to Cite This Article**
Alotaibi TN, Alanazi A. Systematic review of tetracyclines in the treatment of periodontal pockets: Efficacy, applications, and future directions. International Journal of Applied Dental Sciences. 2026;12(1):89-96.