

Mesotherapy in Periodontics: A Narrative Review

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Abstract

Review Article

Introduction: Periodontal diseases are prevalent chronic inflammatory disorders affecting the tooth-supporting apparatus and remain a substantial clinical burden despite established therapeutic approaches. Mesotherapy, defined as the localized microinjection of pharmacologic or bioactive agents into target tissues, has emerged as a minimally invasive adjunctive strategy with potential relevance in periodontal care. **Methods:** A narrative review was conducted through electronic searches of major databases for English-language publications available up to December 2025. Search terms included mesotherapy, periodontitis, gingivitis, periodontal regeneration, local drug delivery, intra-gingival injection, and gingival depigmentation. Eligible literature comprised preclinical studies, clinical trials, case reports, case series, and relevant review articles addressing periodontal inflammation, regenerative outcomes, or gingival esthetics. Owing to marked heterogeneity in study design, interventions, and outcome measures, findings were synthesized narratively. **Results:** The available evidence suggests that mesotherapy may confer localized anti-inflammatory, wound-healing, regenerative, and esthetic benefits in selected periodontal applications. Reported agents include vitamin C, hyaluronic acid, growth factors, platelet-rich plasma, glutathione, tranexamic acid, and antioxidant formulations. Early studies indicate possible reductions in gingival inflammation, improved tissue healing, enhanced patient comfort, and favorable outcomes in gingival depigmentation. Proposed mechanisms include targeted local delivery, modulation of inflammatory pathways, and stimulation of reparative cellular responses. **Discussion:** Mesotherapy is biologically plausible and clinically promising, but the current evidence remains preliminary and methodologically heterogeneous. Standardized protocols, adequately powered randomized controlled trials, and long-term follow-up are required before mesotherapy can be integrated into routine periodontal practice.

Keywords: Mesotherapy; periodontics; periodontitis; gingivitis; local drug delivery; minimally invasive therapy; periodontal regeneration; gingival depigmentation.

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1. INTRODUCTION

1.1 Rationale

Periodontal diseases are chronic biofilm-associated inflammatory disorders that result in progressive destruction of the periodontal ligament, connective tissue attachment, and alveolar bone. Their clinical significance extends beyond tooth loss, as periodontal inflammation has also been associated with systemic conditions such as diabetes mellitus and cardiometabolic disease. Despite substantial advances in scaling and root planing, surgical therapy, and regenerative techniques, clinical limitations remain in anatomically complex sites, deep periodontal pockets, persistent inflammation, and esthetically sensitive areas.

These limitations have created sustained interest in adjunctive treatment approaches capable of delivering therapeutic agents directly to diseased tissues while minimizing systemic exposure. Mesotherapy, originally described as a localized microinjection technique in medicine, has recently been investigated in dentistry as a potential means of delivering anti-inflammatory, antioxidant, regenerative, and esthetic agents into gingival and periodontal tissues.

1.2 Objectives

The objective of this narrative review was to critically evaluate the available literature on mesotherapy in periodontology using a PICOS-framed approach. The review asked whether, in patients or experimental

models with periodontal inflammation, periodontal defects, or gingival hyperpigmentation (P), localized mesotherapeutic administration of bioactive agents (I), compared with conventional therapy, alternative local interventions, or no active comparator (C), improves clinical, histologic, esthetic, or patient-reported outcomes (O) across preclinical and clinical study designs (S). The review further aimed to examine the biologic rationale, summarize current evidence, compare mesotherapy with conventional therapies, and identify major translational barriers and future research priorities.

2. METHODS

2.1 Review design

This article was prepared as a narrative review. A narrative approach was selected because the available literature on periodontal mesotherapy remains limited, emerging, and highly heterogeneous, consisting of mixed study designs including animal studies, case series, case reports, pilot studies, and small clinical trials.

2.2 Eligibility criteria

Studies were considered eligible if they met one or more of the following criteria: involved human participants or animal models relevant to periodontal or gingival tissues; evaluated mesotherapy or localized microinjection of bioactive/pharmacologic agents; and reported inflammatory, regenerative, esthetic, clinical, histologic, or patient-centered outcomes. Randomized trials, comparative clinical studies, pilot studies, case series, case reports, animal studies, and supportive review articles were considered.

Studies were excluded if they lacked oral or periodontal relevance, did not assess mesotherapeutic or comparable localized injection-based interventions, were duplicate reports, or contained insufficient methodological or outcome data. The search was limited to English-language literature published up to December 2025.

2.3 Information sources

Electronic searches were performed in PubMed, Scopus, Web of Science, and Google Scholar. In addition, manual screening of reference lists from relevant articles was undertaken to identify potentially eligible studies not captured in the database searches. The final search update was completed in December 2025.

2.4 Search strategy

The search strategy used combinations of free-text keywords and subject terms, including: "mesotherapy," "periodontitis," "gingivitis," "periodontal disease," "periodontal regeneration," "local drug delivery," "intra-gingival injection," "intramucosal injection," and "gingival depigmentation." A representative search strategy was as follows:

("mesotherapy" OR "local microinjection" OR "intra-gingival injection" OR "intramucosal injection") AND ("periodontitis" OR "gingivitis" OR "periodontal disease" OR "periodontal regeneration" OR "gingival inflammation" OR "gingival depigmentation")

2.5 Study selection

Study selection was performed in two stages: initial screening of titles and abstracts followed by full-text review of potentially eligible articles. Studies were included when they directly addressed periodontal or gingival applications of mesotherapy or localized oral microinjection. For reporting transparency, the search process identified 34 records, 24 remained after removal of duplicates and clearly irrelevant titles, 14 full-text articles were assessed, and 8 studies were included in the final narrative synthesis. Main reasons for exclusion were non-periodontal relevance, absence of a true mesotherapeutic intervention, insufficient methodological detail, or duplication of content.

2.6 Data collection process and data items

Data were extracted manually into a structured summary framework. The following variables were sought where available: author, year, study design, sample size, population or model, indication, intervention agent, concentration, route, dosage, treatment protocol, comparator, follow-up duration, primary outcomes, adverse effects, and major limitations. Funding sources were inconsistently reported in the available literature and therefore could not be assessed systematically.

2.7 Risk of bias and synthesis

Formal pooled risk-of-bias scoring was not feasible because of marked heterogeneity in study designs and incomplete reporting. Instead, a narrative critical appraisal was undertaken at the study level, considering sample size, comparator quality, protocol clarity, follow-up duration, outcome definition, and reproducibility. Because of the diversity of interventions and outcomes, the findings were synthesized narratively.

3. Principles and Mechanisms of Mesotherapy in Periodontology

The therapeutic rationale of mesotherapy is based on targeted local drug delivery combined with biologic tissue stimulation. By introducing active agents directly into gingival or submucosal tissues, mesotherapy may achieve high local therapeutic concentrations while limiting systemic exposure. This is particularly relevant in periodontology, where disease activity is site-specific and strongly influenced by the local inflammatory microenvironment.

In addition to pharmacologic action, the needle puncture itself may contribute to a controlled microtrauma response, stimulating vascular changes, fibroblast activation, collagen synthesis, and local

remodeling. In principle, this dual action may support both symptom control and tissue repair.

Commonly proposed agents for periodontal mesotherapy include hyaluronic acid, growth factors, platelet-rich plasma, antioxidant formulations, and vitamin C. Hyaluronic acid may support extracellular matrix organization and wound healing. Growth factors and platelet-derived products may stimulate angiogenesis and cellular proliferation. Vitamin C is of particular interest because of its role in collagen synthesis, antioxidant defense, and inflammatory modulation.

4. Clinical Applications and Evidence

The current periodontal literature on mesotherapy can be grouped into three principal domains: adjunctive anti-inflammatory use, regenerative support, and gingival depigmentation. (Table 1)

4.1 Mesotherapy as an adjunct to conventional periodontal therapy

Preliminary reports suggest that local injection of vitamin C or related agents may improve selected inflammatory parameters in persistent gingival inflammation and may serve as an adjunct to scaling and root planing. However, the available evidence is largely exploratory and based on case series or pilot-level investigations. Thus, mesotherapy cannot presently be

considered a replacement for conventional periodontal instrumentation.

4.2 Mesotherapy for periodontal regeneration

The regenerative application of mesotherapy remains conceptually attractive but clinically underdeveloped. Animal and biologically oriented studies suggest that local delivery of hyaluronic acid, growth factors, and platelet-derived products may support connective tissue repair and potentially enhance regenerative signaling. Nevertheless, direct evidence for predictable formation of new cementum, periodontal ligament, and alveolar bone in humans remains insufficient.

4.3 Mesotherapy in gingival depigmentation

Among all currently described dental applications, gingival depigmentation has the most clearly documented mesotherapeutic evidence. Published case series and randomized trials have demonstrated that locally injected vitamin C, alone or in combination regimens, may reduce melanin pigmentation with acceptable patient comfort and high esthetic satisfaction. Comparative studies indicate that mesotherapy may be less invasive and better accepted by some patients than surgical depigmentation, although laser therapy may produce faster or more pronounced early outcomes in selected cases.

Table 1: Summary of clinical studies on mesotherapy for gingival depigmentation

Study (Authors and Year)	Study Design	Sample Size	Agents and Protocol	Primary Findings	Key Limitations/Notes
Dawar <i>et al</i>, 2022 [18]	Preliminary case study / case series	6 patients (11 arches)	Vitamin C (1.5-2 mL) with microneedling once weekly for 4 sessions	Significant reduction in pigmentation intensity, improved gingival color, low pain and itching scores, and possible increase in gingival thickness	Small uncontrolled case series; findings require validation with larger samples and longer follow-up
Esmat <i>et al</i>, 2023 [19]	Randomized clinical trial	26 healthy non-smoker individuals	Group I: Vitamin C mesotherapy (L-ascorbic acid 1000 mg/5 mL); Group II: diode laser (980 nm, 1.5 W)	Both modalities were effective; laser showed earlier and greater improvement, whereas mesotherapy was cost-effective, minimally invasive, and satisfactory to patients	Short-term follow-up (3 months)
Haque <i>et al</i>, 2024 [20]	Randomized clinical trial (active controlled)	42 patients (21 per group)	Group I: Locally injected 10% vitamin C, 1.25 mL per quadrant, weekly for up to 4 sessions; Group II: surgical depigmentation	Both approaches were successful and comparable in effectiveness; patient satisfaction was significantly higher in the vitamin C group	Single-center trial; long-term validation needed

Vyas <i>et al</i> , 2025 [21]	Case series	2 patients	Glutathione + tranexamic acid + vitamin C (1:1:1 ratio), 1-1.5 cc intramucosal injection	Significant reduction in pigmentation with satisfactory esthetic improvement at 3 months; no adverse effects or recurrence during follow-up	Very small sample and short follow-up
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5. Comparison with Conventional Therapies

To define the possible role of mesotherapy, it is essential to compare it with established periodontal treatment modalities. Conventional therapies retain the

strongest evidence base and remain the standard of care, whereas mesotherapy currently occupies an exploratory adjunctive position. (Table 2)

Table 2: Comparison of mesotherapy with conventional periodontal therapies

Feature/Aspect	Scaling and Root Planing (SRP)	Periodontal Surgery (Flap)	Local Drug Delivery	Mesotherapy
Invasiveness	Minimally invasive	Moderately to highly invasive	Minimally invasive	Minimally invasive
Target area	Subgingival plaque and calculus	Deep pockets and bone defects	Localized pocket	Localized tissue layers
Mechanism	Mechanical debridement	Mechanical debridement, recontouring, regeneration	Sustained drug release	Targeted drug delivery and tissue stimulation
Healing	By repair	By repair and/or regeneration	Adjunctive to repair	Potential for repair and regeneration
Pain/Discomfort	Mild to moderate	Moderate to severe postoperatively	Minimal	Mild injection-site discomfort
Side effects	Transient sensitivity	Swelling, pain, recession, sensitivity	Local irritation, possible antimicrobial resistance with some agents	Bruising, swelling, rare infection, allergic reaction
Cost	Moderate	High	Moderate to high	Variable depending on agent and session frequency
Evidence level	High	High	Moderate to high	Low, emerging, exploratory
Indications	Gingivitis, mild to moderate periodontitis	Moderate to severe periodontitis, regenerative needs	Localized deep pockets, adjunctive to SRP	Adjunctive to conventional therapy, esthetic or biologic applications
Long-term efficacy	Well established	Well established	Established for selected agents	Limited data

6. Advantages, Disadvantages, Indications, and Contraindications

A critical appraisal of mesotherapy requires balanced consideration of its potential benefits as well as its practical limitations and clinical boundaries. (Table 3)

Table 3: Advantages, disadvantages, indications, and contraindications of mesotherapy in periodontology

Category	Advantages	Disadvantages	Indications	Contraindications
General	Minimally invasive; reduced discomfort and faster recovery than surgery	Lack of standardized protocols for agent selection, concentration, and frequency	Adjunct to conventional periodontal therapy	Uncontrolled systemic diseases
	Targeted local drug delivery with reduced systemic exposure	Limited long-term efficacy data	Localized chronic periodontitis or persistent site-specific inflammation	Acute periodontal infection or abscess

Clinical	Potential to support repair and regeneration	Variable outcomes because of heterogeneous protocols and patient response	Regenerative procedures with biomaterials or biologics	Known allergy to injected substances
Clinical	Favorable patient comfort and acceptance	Risk of bruising, swelling, pain, or local infection	Refractory cases with incomplete response to conventional therapy	Immunosuppressed patients
Regulatory	Possible reduction in need for systemic antibiotics in selected contexts	Regulatory uncertainty and off-label use concerns	Postoperative or chronic inflammatory pain modulation	Pregnancy and lactation unless specifically justified
Economic	Potential office-based delivery	Cost may exceed conventional therapy depending on protocol complexity	Selected esthetic applications such as gingival depigmentation	Situations with poor cost-benefit justification

7. DISCUSSION

7.1 First key concept: Biological plausibility versus clinical proof

The major strength of mesotherapy is its biologic plausibility. Site-specific injection aligns conceptually with the localized nature of periodontal inflammation and with the need for targeted therapeutic delivery. Available studies suggest potential benefit in gingival inflammation control, tissue healing, and depigmentation. However, the strength of evidence remains low to moderate because most studies are small, single-center, short-term, or observational in nature.

Conflicting findings also exist. Although mesotherapy may provide outcomes comparable to surgical depigmentation with higher patient satisfaction, laser-based techniques may produce faster or superior early results in some studies. These variations likely reflect differences in pigmentation severity, drug formulations, operator technique, and follow-up duration. Future research should directly compare modalities using standardized outcome measures and longer observation periods.

7.2 Second key concept: Standardization as the principal translational barrier

The most important obstacle to broader clinical use of mesotherapy is the absence of standardized treatment protocols. Current studies vary widely in injected agent, concentration, volume, injection depth, frequency of administration, and clinical endpoints. This prevents meaningful cross-study comparison and limits reproducibility.

For clinicians, this means that mesotherapy should currently be regarded as an adjunctive, selective, and investigational option rather than a routine therapeutic recommendation. For researchers and policy makers, the priority should be the development of reproducible protocols, multicenter randomized controlled trials, harmonized outcome measures, detailed safety reporting, and long-term comparative effectiveness studies.

7.3 Limitations

This review has limitations at both the study and review levels. At the study level, most available reports involve small cohorts, limited controls, short follow-up, and substantial protocol heterogeneity. Risk of bias is likely significant, especially in case-based and non-randomized evidence. At the review level, restriction to English-language literature may have excluded relevant studies, and the narrative design, although appropriate for the current state of evidence, does not provide the exhaustive methodological rigor of a formal systematic review.

8. CONCLUSION

Mesotherapy is an emerging and minimally invasive adjunctive strategy with potential relevance to periodontal inflammation control, soft-tissue healing, regenerative support, and gingival depigmentation. The most promising current evidence lies in esthetic gingival applications and localized anti-inflammatory use, whereas evidence supporting predictable periodontal regeneration remains insufficient. At present, mesotherapy should be interpreted as investigational rather than standard periodontal care. Future research must prioritize standardized protocols, robust comparative trial designs, validated outcome measures, and long-term follow-up to establish whether mesotherapy can assume a reliable place in evidence-based periodontology.

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