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# BEYOND TOMATOES: LYCOPENE AS AN ADJUNCT IN PERIODONTAL INFLAMMATION CONTROL

# ALÉM DOS TOMATES: O LICOPENO COMO ADJUNTO NO CONTROLE DA INFLAMAÇÃO PERIODONTAL

# MÁS ALLÁ DE LOS TOMATES: EL LICOPENO COMO COADYUVANTE EN EL CONTROL DE LA INFLAMACIÓN PERIODONTAL

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## ABSTRACT

**Objective:** To evaluate the role of lycopene as an adjunctive agent in periodontal therapy, focusing on its antioxidant and anti-inflammatory effects on periodontal parameters.

**Methods:** A narrative review of experimental and clinical studies investigating lycopene supplementation in patients with periodontitis was conducted.

**Results:** Available evidence suggests that lycopene exhibits significant antioxidant properties capable of reducing oxidative stress associated with periodontal disease. Clinical studies indicate improvements in key periodontal parameters, including reductions in gingival inflammation, BOP, and PD, when lycopene is used as an adjunct to conventional periodontal therapy. Additionally, modulation of inflammatory mediators and decreased levels of reactive oxygen species were observed, supporting its biological plausibility.

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**Conclusion:** Lycopene shows potential as a beneficial adjunct in periodontal therapy by targeting oxidative stress and inflammation. Although current findings are promising, the heterogeneity of study designs and limited number of high-quality randomized clinical trials warrant further research to establish standardized protocols and confirm long-term clinical benefits.

**Keywords:** Lycopene. Periodontitis. Oxidative Stress. Antioxidants. Inflammation. Adjunctive Therapy. Periodontal Treatment.

**RESUMO**

**Objetivo:** Avaliar o papel do licopeno como adjuvante na terapia periodontal, com foco em seus efeitos antioxidantes e anti-inflamatórios sobre os parâmetros periodontais.

**Métodos:** Foi realizada uma revisão narrativa de estudos experimentais e clínicos que investigaram a suplementação com licopeno em pacientes com periodontite.

**Resultados:** As evidências disponíveis sugerem que o licopeno apresenta propriedades antioxidantes significativas, capazes de reduzir o estresse oxidativo associado à doença periodontal. Estudos clínicos indicam melhorias em parâmetros periodontais importantes, incluindo redução da inflamação gengival, sangramento à sondagem (SS) e profundidade de sondagem (PS), quando o licopeno é utilizado como adjuvante à terapia periodontal convencional. Além disso, observou-se modulação de mediadores inflamatórios e diminuição dos níveis de espécies reativas de oxigênio, corroborando sua plausibilidade biológica.

**Conclusão:** O licopeno demonstra potencial como adjuvante benéfico na terapia periodontal, atuando no combate ao estresse oxidativo e à inflamação. Embora os achados atuais sejam promissores, a heterogeneidade dos desenhos dos estudos e o número limitado de ensaios clínicos randomizados de alta qualidade justificam pesquisas adicionais para estabelecer protocolos padronizados e confirmar os benefícios clínicos a longo prazo.

**Palavras-chave:** Licopeno. Periodontite. Estresse Oxidativo. Antioxidantes. Inflamação. Terapia Adjuvante. Tratamento Periodontal.

**RESUMEN**

**Objetivo:** Evaluar el papel del licopeno como coadyuvante en la terapia periodontal, centrándonos en sus efectos antioxidantes y antiinflamatorios sobre los parámetros periodontales.

**Métodos:** Se realizó una revisión narrativa de estudios experimentales y clínicos que investigaron la suplementación con licopeno en pacientes con periodontitis.

**Resultados:** La evidencia disponible sugiere que el licopeno presenta importantes propiedades antioxidantes capaces de reducir el estrés oxidativo asociado a la enfermedad periodontal. Los estudios clínicos indican mejoras en parámetros periodontales clave, incluyendo reducciones en la inflamación gingival, el sangrado al sondaje (BOP) y la profundidad de sondaje (PD), cuando el licopeno se utiliza como coadyuvante a la terapia periodontal convencional. Además, se observó modulación de mediadores inflamatorios y disminución de los niveles de especies reactivas de oxígeno, lo que respalda su plausibilidad biológica.

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**Conclusión:** El licopeno muestra potencial como coadyuvante beneficioso en la terapia periodontal al actuar sobre el estrés oxidativo y la inflamación. Si bien los hallazgos actuales son prometedores, la heterogeneidad de los diseños de estudio y el número limitado de ensayos clínicos aleatorizados de alta calidad justifican la necesidad de realizar más investigaciones para establecer protocolos estandarizados y confirmar los beneficios clínicos a largo plazo.

**Palabras clave:** Licopeno. Periodontitis. Estrés Oxidativo. Antioxidantes. Inflamación. Terapia Coadyuvante. Tratamiento Periodontal.

## 1 INTRODUCTION

Periodontitis is a multifactorial chronic inflammatory disease characterized by the progressive destruction of the tooth-supporting structures, including the periodontal ligament and alveolar bone. Its pathogenesis is driven by a dysbiotic shift in the oral microbiome, leading to a sustained host immune-inflammatory response that ultimately results in tissue breakdown (Hajishengallis, 2015). While the microbial challenge is essential for disease initiation, it is now well established that host-mediated mechanisms, particularly oxidative stress play a central role in disease progression.

Oxidative stress arises from an imbalance between the production of reactive oxygen species (ROS) and the capacity of antioxidant defense systems. In periodontal tissues, excessive ROS production is primarily associated with hyperactive neutrophils and other immune cells responding to bacterial biofilm (Chapple & Matthews, 2007). These reactive molecules contribute to lipid peroxidation, protein degradation, and DNA damage, amplifying tissue injury and perpetuating inflammation. Importantly, oxidative stress has been recognized not only as a consequence but also as a driving factor in periodontal disease, reinforcing a self-sustaining cycle of inflammation and tissue destruction (Sczepanik et al., 2020).

Given this pathophysiological framework, therapeutic strategies targeting oxidative pathways have gained increasing attention. Conventional periodontal therapy, particularly scaling and root planing, effectively reduces bacterial load; however, it does not fully address the host-mediated inflammatory and oxidative components of the disease. This limitation has led to growing interest in adjunctive approaches aimed at modulating host response, including the use of antioxidant compounds.

Lycopene, a non-provitamin A carotenoid predominantly found in tomatoes and other red-colored fruits, has emerged as one of the most potent natural antioxidants. Its molecular structure, characterized by an extended system of conjugated double bonds, allows it to efficiently quench singlet oxygen and neutralize free radicals (Rao & Agarwal, 2000). In fact, lycopene has been reported to exhibit higher singlet oxygen-quenching capacity compared to other carotenoids and traditional antioxidants.

Beyond its antioxidant activity, lycopene also exerts anti-inflammatory effects through modulation of key signaling pathways. Experimental studies suggest that lycopene can inhibit nuclear factor kappa B (NF-κB) activation, reduce the expression of pro-inflammatory cytokines, and downregulate enzymes involved in inflammatory processes (Story et al., 2010). These properties are particularly relevant in periodontitis, where dysregulated inflammatory responses contribute significantly to tissue destruction.

Clinical investigations have begun to explore the potential application of lycopene in periodontal therapy. Evidence suggests that its use as an adjunct to conventional treatment may enhance clinical outcomes, including reductions in gingival inflammation, bleeding on probing, and probing depth (Chandra et al., 2007; Arora et al., 2013). These findings support the concept that dietary or supplemental antioxidants can influence periodontal health by targeting both local and systemic inflammatory pathways.

Furthermore, the integration of nutritional factors into periodontal care reflects a broader paradigm shift toward a more holistic understanding of oral health, recognizing the interplay between diet, systemic conditions, and inflammatory diseases. Lycopene, in this context, represents a promising candidate for adjunctive therapy due to its safety profile, accessibility, and biological plausibility.

Despite these encouraging findings, the current body of evidence remains limited by heterogeneity in study designs, variations in dosage and administration protocols, and relatively small sample sizes. Therefore, further well-designed studies are required to clarify its therapeutic efficacy, optimal use, and long-term benefits in periodontal treatment.

## 2 METHODOLOGY

This study was designed as a narrative review aimed at synthesizing current evidence on the role of lycopene in periodontal disease. A comprehensive search was conducted in PubMed/MEDLINE, Scopus, and Web of Science using combinations of the terms “lycopene,” “periodontitis,” “oxidative stress,” and “inflammation.”

Studies of different designs were considered eligible, including experimental, clinical, and translational research, as well as relevant in vitro investigations that contributed to the understanding of biological mechanisms. No strict restrictions were applied regarding study design in order to provide a broad overview of available evidence.

The selection process prioritized studies addressing antioxidant activity, inflammatory modulation, and the potential role of lycopene in periodontal contexts.

Data were extracted focusing on general study characteristics, type of evidence, and main contributions to the topic. The findings were organized into thematic categories, including biological mechanisms, experimental evidence, and potential clinical implications. A qualitative synthesis was performed.

## 3 RESULTS

The available evidence on lycopene as an adjunct in periodontal therapy was organized into three main domains: (1) antioxidant effects, (2) anti-inflammatory mechanisms, and (3) clinical periodontal outcomes.

### 3.1 ANTIOXIDANT EFFECTS OF LYCOPENE IN PERIODONTAL CONTEXTS

Across experimental and clinical studies, lycopene consistently demonstrated strong antioxidant capacity, primarily through its ability to neutralize reactive oxygen species (ROS). Its molecular structure, rich in conjugated double bonds, allows efficient quenching of singlet oxygen and inhibition of free radical-mediated damage (Rao & Agarwal, 2000).

In periodontal settings, oxidative stress markers were found to be significantly reduced following lycopene supplementation. Studies reported decreases in lipid peroxidation products and improvements in total antioxidant capacity, suggesting a restoration of redox balance in periodontal tissues (Chapple & Matthews, 2007). This is particularly relevant given that excessive ROS production by neutrophils plays a central role in periodontal tissue breakdown.

Additionally, experimental evidence supports that lycopene can protect cellular components from oxidative damage, including DNA and proteins, thereby limiting the progression of periodontal destruction (Sczepanik et al., 2020).

### 3.2 MODULATION OF INFLAMMATORY PATHWAYS

Beyond its antioxidant activity, lycopene has been shown to exert significant anti-inflammatory effects. Mechanistic studies indicate that lycopene inhibits the activation of nuclear factor kappa B, a key transcription factor involved in the regulation of inflammatory responses (Story et al., 2010).

This inhibition leads to reduced expression of pro-inflammatory cytokines such as interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α), both of which are critically involved in periodontal tissue destruction. Furthermore, lycopene has been associated with downregulation of inflammatory enzymes and mediators, contributing to a less destructive inflammatory environment.

These findings reinforce the concept that lycopene acts not only as a passive antioxidant but also as an active modulator of host immune response, directly targeting pathways implicated in periodontitis pathogenesis (Hajishengallis, 2015).

### 3.3 CLINICAL OUTCOMES IN PERIODONTAL THERAPY

Clinical studies evaluating lycopene as an adjunct to conventional periodontal therapy, particularly scaling and root planing (SRP) reported improvements in key periodontal parameters.

Randomized and controlled trials demonstrated significant reductions in:

- Gingival inflammation
- Bleeding on probing (BOP)
- Probing depth (PD)

When lycopene supplementation was combined with SRP compared to SRP alone (Arora et al., 2013; Chandra et al., 2007).

In patients with gingivitis, lycopene administration resulted in a marked reduction in gingival index scores, suggesting its effectiveness even in early stages of periodontal disease (Chandra et al., 2007). In chronic periodontitis patients, adjunctive lycopene led to enhanced clinical improvements, supporting its role in more advanced conditions (Arora et al., 2013).

Importantly, these clinical benefits were observed without significant adverse effects, reinforcing the safety profile of lycopene as a therapeutic adjunct.

### 3.4 SUMMARY OF EVIDENCE

Overall, the evidence indicates that lycopene contributes to periodontal health through a dual mechanism:

- Reduction of oxidative stress
- Modulation of inflammatory responses

These biological effects translate into measurable clinical improvements when used alongside conventional periodontal therapy. However, variability in study design, dosage, and duration limits direct comparability across studies and highlights the need for standardized clinical protocols.

## 4 DISCUSSION

The present review highlights lycopene as a promising adjunctive agent in periodontal therapy, primarily due to its dual antioxidant and anti-inflammatory properties. The findings suggest that its biological effects are not merely supportive but may actively interfere with key pathogenic mechanisms underlying periodontitis.

From a pathophysiological perspective, the role of oxidative stress in periodontal destruction has been increasingly recognized as central rather than secondary. Reactive oxygen species (ROS), produced by hyperactive neutrophils, contribute to connective tissue breakdown and alveolar bone resorption. In this context, antioxidant strategies have emerged as a logical extension of conventional mechanical therapy. Lycopene, due to its superior singlet oxygen–quenching capacity, appears particularly well-suited to counteract oxidative imbalance (Krinsky & Johnson, 2005).

Importantly, the benefits of lycopene extend beyond direct ROS scavenging. Evidence suggests that oxidative stress and inflammation are tightly interconnected processes, with redox imbalance acting as a trigger for intracellular signaling cascades. Lycopene has been shown to interfere with these pathways, including inhibition of nuclear factor kappa B (NF-κB) and modulation of mitogen-activated protein kinases (MAPKs), resulting in decreased expression of pro-inflammatory mediators (Palozza et al., 2012). This is highly relevant in periodontitis, where host-mediated inflammation drives much of the tissue destruction.

Another critical aspect is the interaction between systemic and local inflammation. Periodontitis has been increasingly associated with systemic conditions such as diabetes mellitus and cardiovascular diseases, both of which are characterized by chronic low-grade inflammation and oxidative stress. Lycopene has demonstrated systemic anti-inflammatory effects, including reductions in circulating inflammatory biomarkers and improvement of endothelial function (Riccioni et al., 2008). This raises the possibility that its adjunctive use in periodontal therapy could provide benefits that extend beyond the oral cavity, aligning with the concept of periodontal medicine.

Clinically, the improvements observed with lycopene supplementation particularly in gingival inflammation, bleeding on probing, and probing depth are consistent with a host modulation effect. However, these outcomes should be interpreted with caution. Many of the available clinical studies present methodological limitations, including small sample sizes, short follow-up periods, and variability in dosage and mode of administration. Additionally, differences in baseline disease severity and patient-related factors (such as diet and systemic health) may influence treatment response, limiting the generalizability of findings (Basu & Imrhan, 2007).

Another limitation lies in the lack of standardized protocols for lycopene use. Studies have employed different dosages, ranging from dietary intake to pharmacological supplementation, with no consensus on optimal therapeutic levels. Furthermore, the bioavailability of lycopene is influenced by several factors, including food matrix, processing,

and individual metabolic differences, which may impact its clinical efficacy (Stahl & Sies, 2005).

It is also important to consider that while antioxidant supplementation appears beneficial, excessive use of antioxidants may disrupt physiological redox signaling, which is essential for normal cellular function. Therefore, the goal should not be complete suppression of ROS but rather restoration of redox homeostasis. This reinforces the need for carefully designed clinical trials to determine safe and effective therapeutic windows.

Future research should prioritize well-designed randomized controlled trials with larger sample sizes and longer follow-up periods. Standardization of dosage, formulation, and delivery methods is essential to establish clear clinical guidelines. Moreover, the incorporation of molecular biomarkers, such as cytokine profiles, oxidative stress markers, and gene expression analyses would provide deeper insights into the mechanisms of action of lycopene in periodontal tissues.

In addition, exploring the synergistic effects of lycopene with other host-modulating agents, such as omega-3 fatty acids or melatonin, may represent a promising avenue for enhancing therapeutic outcomes. Given the multifactorial nature of periodontitis, combination strategies targeting multiple pathogenic pathways are likely to be more effective than single-agent approaches.

## 5 CONCLUSION

Lycopene emerges as a biologically plausible and clinically promising adjunct in periodontal therapy, primarily due to its capacity to modulate oxidative stress and inflammatory responses, two central mechanisms in the pathogenesis of periodontitis. The current body of evidence suggests that its use alongside conventional periodontal treatment may enhance clinical outcomes, particularly in reducing gingival inflammation, bleeding on probing, and probing depth.

However, despite these encouraging findings, the available evidence remains limited by methodological heterogeneity, small sample sizes, and lack of standardized therapeutic protocols. Variations in dosage, formulation, and bioavailability further complicate the interpretation and comparability of results.

Therefore, while lycopene represents a safe, accessible, and potentially effective adjunctive strategy, its incorporation into routine periodontal practice should be approached with caution. Future well-designed randomized clinical trials with standardized methodologies and long-term follow-up are essential to confirm its efficacy, establish optimal dosing regimens, and clarify its role within the broader framework of host modulation therapy.

Ultimately, the integration of nutraceuticals such as lycopene into periodontal care reflects an evolving paradigm that emphasizes not only microbial control but also the regulation of host response, opening new avenues for more comprehensive and personalized treatment approaches.

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