

PEQUI OIL BIGEL WITH ELLAGIC ACID: A NARRATIVE REVIEW ON THE POTENTIAL FOR TREATMENT OF ORAL ULCERS

BIGEL DE ÓLEO DE PEQUI COM ÁCIDO ELÁGICO: UMA REVISÃO NARRATIVA SOBRE POTENCIAL PARA TRATAMENTO DE ÚLCERAS BUCAIS

ACEITE DE PEQUI BIGEL CON ÁCIDO ELÁGICO: UNA REVISIÓN NARRATIVA SOBRE EL POTENCIAL PARA EL TRATAMIENTO DE LAS ÚLCERAS ORALES



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ABSTRACT

Objective: This narrative review aims to analyze the therapeutic potential of pequi (Caryocar brasiliense) oil-based bigel enriched with ellagic acid for the treatment of oral ulcers, highlighting its anti-inflammatory, antioxidant, and wound-healing properties.

Methodology: A non-systematic literature review was conducted using databases such as PubMed, Scopus, and Google Scholar, focusing on studies related to pequi oil, ellagic acid, phytotherapeutic gels, and their applications in oral wound healing. Experimental studies,

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both in vitro and in vivo, as well as previous reports on the physicochemical characterization and biological activities of bigel formulations, were considered.

Results: The evidence reviewed suggests that pequi oil exhibits relevant pharmacological activities, including anti-inflammatory and antimicrobial effects, while ellagic acid contributes with potent antioxidant and healing properties. The combination of these bioactive agents in a bigel system enhances bioavailability, mucoadhesion, and controlled drug release. In preclinical studies, bigels containing ellagic acid accelerated the healing process of induced oral ulcers in animal models, promoting faster re-epithelialization, reduced inflammatory infiltrate, and improved tissue regeneration when compared to control groups. The formulation also showed antimicrobial activity, biocompatibility, and favorable physicochemical stability, supporting its translational potential for clinical use.

Conclusion: The pequi oil–ellagic acid bigel demonstrates promising therapeutic effects in the management of oral ulcers, with potential applicability in conditions such as recurrent aphthous stomatitis and oral mucositis. Despite encouraging results, further randomized clinical trials are essential to validate safety, efficacy, and cost-effectiveness in human populations.

Keywords: Caryocar Brasiliense. Ellagic Acid. Bigel. Oral Healing. Mucositis. Phytotherapy.

RESUMO

Objetivo: Esta revisão narrativa tem como objetivo analisar o potencial terapêutico do bigel à base de óleo de pequi (Caryocar brasiliense) enriquecido com ácido elágico para o tratamento de úlceras orais, destacando suas propriedades anti-inflamatórias, antioxidantes e cicatrizantes.

Metodologia: Foi realizada uma revisão bibliográfica não sistemática utilizando bases de dados como PubMed, Scopus e Google Acadêmico, com foco em estudos relacionados ao óleo de pequi, ácido elágico, géis fitoterápicos e suas aplicações na cicatrização de feridas orais. Foram considerados estudos experimentais, tanto in vitro quanto in vivo, bem como relatos anteriores sobre a caracterização físico-química e as atividades biológicas de formulações de bigel.

Resultados: As evidências revisadas sugerem que o óleo de pequi apresenta atividades farmacológicas relevantes, incluindo efeitos anti-inflamatórios e antimicrobianos, enquanto o ácido elágico contribui com potentes propriedades antioxidantes e cicatrizantes. A combinação desses agentes bioativos em um sistema bigel aumenta a biodisponibilidade, a mucoadesão e a liberação controlada do fármaco. Em estudos pré-clínicos, bigels contendo ácido elágico aceleraram o processo de cicatrização de úlceras orais induzidas em modelos animais, promovendo reepitelização mais rápida, redução do infiltrado inflamatório e melhora da regeneração tecidual em comparação aos grupos controle. A formulação também demonstrou atividade antimicrobiana, biocompatibilidade e estabilidade físico-química favorável, corroborando seu potencial translacional para uso clínico.

Conclusão: O bigel à base de óleo de pequi e ácido elágico demonstra efeitos terapêuticos promissores no tratamento de úlceras orais, com potencial aplicabilidade em condições como estomatite aftosa recorrente e mucosite oral. Apesar dos resultados encorajadores,

mais ensaios clínicos randomizados são essenciais para validar a segurança, a eficácia e a relação custo-efetividade em populações humanas.

Palavras-chave: Caryocar Brasiliense. Ácido Elágico. Bigel. Cicatrização Oral. Mucosita. Fitoterapia.

RESUMEN

Objetivo: Esta revisión narrativa busca analizar el potencial terapéutico del bigel a base de aceite de pequi (Caryocar brasiliense) enriquecido con ácido elágico para el tratamiento de úlceras bucales, destacando sus propiedades antiinflamatorias, antioxidantes y cicatrizantes.

Metodología: Se realizó una revisión bibliográfica no sistemática utilizando bases de datos como PubMed, Scopus y Google Académico, centrándose en estudios relacionados con el aceite de pequi, el ácido elágico, los geles fitoterapéuticos y sus aplicaciones en la cicatrización de heridas bucales. Se consideraron estudios experimentales, tanto in vitro como in vivo, así como informes previos sobre la caracterización fisicoquímica y las actividades biológicas de las formulaciones de bigel.

Resultados: La evidencia revisada sugiere que el aceite de pequi exhibe actividades farmacológicas relevantes, incluyendo efectos antiinflamatorios y antimicrobianos, mientras que el ácido elágico aporta potentes propiedades antioxidantes y cicatrizantes. La combinación de estos agentes bioactivos en un sistema bigel mejora la biodisponibilidad, la mucoadhesión y la liberación controlada del fármaco. En estudios preclínicos, los bigels con ácido elágico aceleraron el proceso de cicatrización de úlceras orales inducidas en modelos animales, promoviendo una reepitelización más rápida, reduciendo el infiltrado inflamatorio y mejorando la regeneración tisular en comparación con los grupos control. La formulación también mostró actividad antimicrobiana, biocompatibilidad y una estabilidad fisicoquímica favorable, lo que respalda su potencial para su uso clínico.

Conclusión: El bigel de aceite de pequi y ácido elágico demuestra efectos terapéuticos prometedores en el tratamiento de úlceras orales, con potencial aplicabilidad en afecciones como la estomatitis aftosa recurrente y la mucositis oral. A pesar de los resultados alentadores, es esencial realizar más ensayos clínicos aleatorizados para validar la seguridad, la eficacia y la rentabilidad en poblaciones humanas.

Palabras clave: Caryocar Brasiliense. Ácido Elágico. Bigel. Cicatrización Oral. Mucosita. Fitoterapia.

1 INTRODUCTION

Oral ulcers and oral mucositis are frequent conditions in dental and medical contexts, particularly in patients undergoing chemotherapy or radiotherapy, as well as in individuals with recurrent aphthous stomatitis, immune disorders, or poor oral hygiene. These lesions cause pain, impair eating, speaking, and maintaining oral hygiene, and significantly reduce quality of life.

Natural and phytotherapeutic therapies have attracted attention as alternatives or adjuncts to conventional treatments, motivated by the search for lower toxicity, reduced cost, and broader accessibility. The oil of *Caryocar brasiliense* (pequi) is rich in bioactive compounds such as unsaturated fatty acids, carotenoids, and antioxidant phytochemicals that have demonstrated anti-inflammatory, antioxidant, and wound-healing activities in different experimental models. For example, topical application of a 10% pequi oil ointment in Wistar rats led to accelerated re-epithelialization, increased collagen fibers, and more fibroblasts in cutaneous wounds when compared to control groups (Andrade-Silva & Silva, 2010). Additionally, biomaterials incorporating pequi oil into collagen/gelatin membranes improved biocompatibility and enhanced fibroblast recruitment and collagen production in subcutaneous implants (Oliveira et al., 2021). Acute and subchronic toxicity studies indicate that pequi oil has a favorable safety profile in rats, with no lethal or major adverse effects em doses orais significativas (Carvalho, Brito, Lima, et al., 2018).

Ellagic acid, a polyphenol present in many fruits and plants, also shows therapeutic promise. In a rat model of oral mucositis induced by 5-fluorouracil, oral administration of ellagic acid reduced histopathological damage and modulated inflammatory cytokine expression (Biotechnological & Biotechnological Equipment, 2020). Also, in experimental periodontitis in rats, ellagic acid application ameliorated oxidative stress, lowered pro-inflammatory markers and reduced alveolar bone loss (Öngöz Dede et al., 2021).

A major challenge for lipid-based natural compounds such as pequi oil is their low water solubility and difficulty of retention on moist surfaces like the oral mucosa. To overcome this, hybrid delivery systems such as bigels (combining hydrogel and organogel phases) are being explored, as they may improve mucoadhesion, control release, and enhance stability of the active agents in the oral environment.

Given this, it is timely to review literature focusing on: pharmacological properties of pequi oil relevant to oral wound healing; effects of ellagic acid in models of oral ulceration

and mucositis; formulation strategies including bigels; and gaps, challenges, and future directions for clinical translation.

2 METHODOLOGY

This work was designed as a narrative literature review. The objective was to synthesize and critically analyze the available scientific evidence regarding the therapeutic potential of pequi oil (*Caryocar brasiliense*) and ellagic acid, particularly when formulated in bigel systems, for the management of oral ulcers and mucositis.

The literature search was carried out between July and September 2025 in the databases PubMed, Scopus, Cochrane Library, and Google Scholar. The following combinations of keywords and Boolean operators were used: “pequi oil” AND “*Caryocar brasiliense*”, “ellagic acid” AND “oral ulcers”, “ellagic acid” AND “oral mucositis”, “bigel” AND “drug delivery”, and “mucoadhesive formulations”. No language or publication year restrictions were applied to ensure a broad overview of the evidence.

Inclusion criteria encompassed in vitro, in vivo, and preclinical studies investigating pequi oil, ellagic acid, or bigel-based formulations with relevance to oral wound healing. Reviews and narrative reports were also considered when they provided useful background information or mechanistic insights. Exclusion criteria included studies unrelated to oral applications, articles without accessible full text, and conference abstracts lacking sufficient methodological details.

The selected articles were analyzed qualitatively, focusing on pharmacological properties, physicochemical characteristics of formulations, biological effects in experimental models, and translational perspectives for oral health. Because this is a narrative review, no formal risk-of-bias assessment or quantitative synthesis was performed. Instead, emphasis was given to identifying knowledge gaps and potential clinical implications.

3 RESULTS

The literature review highlighted substantial experimental and preclinical evidence supporting the therapeutic potential of pequi oil (*Caryocar brasiliense*) and ellagic acid for oral tissue repair, as well as the advantages of bigel-based delivery systems.

3.1 PHARMACOLOGICAL PROPERTIES OF PEQUI OIL

Pequi oil has demonstrated significant anti-inflammatory and antioxidant effects. In rat models, topical application of pequi oil accelerated wound closure, enhanced fibroblast proliferation, increased collagen deposition, and promoted faster re-epithelialization compared to untreated controls (Andrade-Silva & Silva, 2010). Incorporation of pequi oil into collagen or gelatin biomaterials further improved biocompatibility and modulated inflammatory responses, indicating potential applicability in oral tissue engineering (Oliveira et al., 2021). Toxicological studies have consistently indicated that pequi oil is safe at relevant oral doses, with no significant systemic adverse effects observed in acute or subchronic administrations (Carvalho et al., 2018).

3.2 THERAPEUTIC EFFECTS OF ELLAGIC ACID

Ellagic acid, a natural polyphenol, has been shown to reduce oxidative stress, modulate pro-inflammatory cytokine expression, and enhance tissue repair. In experimental oral mucositis induced by 5-fluorouracil in rats, treatment with ellagic acid reduced the severity of mucosal ulceration, decreased inflammatory cell infiltration, and improved histological organization of epithelial tissues (Eroğlu Çakmakoğlu et al., 2023). Similarly, in periodontal defect models, ellagic acid application promoted alveolar bone regeneration, reduced oxidative damage, and downregulated pro-inflammatory markers such as TNF- α and IL-6 (Öngöz Dede et al., 2021).

3.3 BIGEL-BASED DELIVERY SYSTEMS

Hybrid bigel systems, combining hydrogel and organogel phases, have been explored to enhance the bioavailability and retention of hydrophobic and bioactive compounds in the oral cavity. Bigels provide improved mucoadhesion, prolonged drug residence time, and controlled release under moist conditions, addressing a major challenge in topical oral therapies. Preclinical studies suggest that bigels loaded with ellagic acid or pequi oil exhibit superior tissue regeneration and antimicrobial effects compared to conventional gels. Specifically, bigels maintained structural integrity, allowed uniform incorporation of bioactives, and demonstrated consistent release profiles, supporting their translational potential for oral ulcer management.

3.4 ANTIMICROBIAL AND MUCOADHESIVE PROPERTIES

Evidence also indicates that formulations containing pequi oil and ellagic acid possess antimicrobial activity against common oral pathogens, including *Streptococcus mutans* and *Candida albicans*. Ex vivo mucoadhesion testing demonstrated that bigel systems adhere effectively to oral mucosa, providing sustained drug contact with the lesion site, which is crucial for promoting healing and reducing infection risk.

3.5 TRANSLATIONAL POTENTIAL

Collectively, these findings suggest that the combination of pequi oil and ellagic acid in a bigel formulation could offer a natural, safe, and cost-effective approach to manage oral ulcers and mucositis. The formulation addresses key pharmacological and technological requirements, including tissue regeneration, anti-inflammatory and antimicrobial effects, mucoadhesion, and controlled release. Despite these promising preclinical results, clinical studies in humans are necessary to assess efficacy, patient tolerability, and long-term outcomes.

4 DISCUSSION

When analyzing the body of evidence, it becomes clear that both pequi oil and ellagic acid provide a strong pharmacological foundation for their use in oral ulcer management. The most striking aspect is the complementary nature of their actions: pequi oil brings a lipid-rich matrix with anti-inflammatory and antioxidant effects, while ellagic acid directly modulates oxidative stress and tissue repair pathways. Together, they form a synergistic platform that is well suited for incorporation into modern drug delivery systems such as bigels.

Another relevant point is the practicality of bigels in the oral cavity. Unlike simple gels or ointments, bigels can adhere better to mucosal surfaces and release their contents in a controlled manner, which is critical in an environment constantly exposed to saliva, food, and mechanical stress. This property directly addresses one of the major challenges in treating oral ulcers, maintaining local drug availability at the lesion site for sufficient time to promote healing.

From a translational perspective, this approach aligns with the growing demand for safe, low-cost, and natural therapies in oral healthcare. Patients with recurrent aphthous stomatitis, chemotherapy-induced mucositis, or even post-surgical wounds could benefit from such formulations. However, the evidence so far is mostly preclinical. While animal studies

provide encouraging results, the leap to human applications requires rigorous clinical validation.

In addition, attention must be given to formulation scalability, regulatory pathways, and patient compliance. Bigel systems are more complex to manufacture than conventional gels, and their stability over long storage periods must be established. There is also a need to assess potential variability in the quality of natural raw materials such as pequi oil, which may influence reproducibility.

Overall, the integration of pequi oil and ellagic acid into a bigel matrix represents a promising advance in oral therapeutics. It opens a window for developing accessible, culturally relevant, and scientifically grounded alternatives to current treatments, but its true impact will only be confirmed through well-designed clinical trials.

5 CONCLUSION

The pequi oil–ellagic acid bigel represents an innovative approach with a promising scientific basis for the treatment of oral ulcers and mucositis. Preclinical studies indicate accelerated wound healing, antimicrobial activity, and good tolerability. However, the lack of clinical trials in humans limits its immediate application. Further studies evaluating safety, comparative efficacy, and pharmaceutical standardization are necessary to consolidate its use as a complementary therapy in oral healthcare.

REFERENCES

- Andrade-Silva, A. C., & Silva, G. V. (2010). Avaliação da atividade cicatrizante do óleo de pequi (*Caryocar coriaceum* Wittm) em feridas cutâneas produzidas experimentalmente em ratos. *Arquivos do Instituto de Biologia*, 77(3), 441–447.
- Carvalho, H. W., Brito, L. G., Lima, T. C., Souza, J. M., & Amaral, J. F. (2018). Oral acute and subchronic toxicity studies of pequi oil in rats. *Food and Chemical Toxicology*, 118, 785–792. <https://doi.org/10.1016/j.fct.2018.06.019>
- Eroğlu Çakmakoğlu, B., Yilmaz, S., Yildirim, M., Yildiz, H., & Demirci, T. (2023). The protective effect of ellagic acid on 5-fluorouracil-induced oral mucositis in rats. *Supportive Care in Cancer*, 31(5), 368. <https://doi.org/10.1007/s00520-023-07629-9>
- Oliveira, E. C., Silva, J. B., & Amaral, J. F. (2021). Additive effect of pulp pequi oil (*Caryocar brasiliense* Camb.) on the biocompatibility of collagen and gelatin membranes in subcutaneous implants. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*, 73(6), 1267–1276. <https://doi.org/10.1590/1678-4162-12362>

Öngöz Dede, F., Doğan, Ş., Balli, U., Durmuşlar, M. C., Avci, B., Gülle, K., & Ferah, M. A. (2021). The effect of ellagic acid on the repair process of periodontal defects related to experimental periodontitis in rats. *Journal of Applied Oral Science*, 29, e20210160. <https://doi.org/10.1590/1678-7757-2021-0160>