

## Antimicrobial and anti-inflammatory properties and clinical applications of *Plantago major* as an alternative to chlorhexidine in canine periodontitis

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Recibido: 02/10/2025 Aprobado: 05/01/2026

### ABSTRACT

Canine periodontitis is a highly prevalent condition in veterinary practice, with significant consequences for both oral and systemic health. Chlorhexidine (CHX) is the standard antiseptic used in periodontal protocols; however, its application in dogs is limited by adverse effects and by the lack of robust clinical evidence. *Plantago major* (*P. major*) exhibits antimicrobial, anti-inflammatory, and wound-healing properties. The aim of this review was to evaluate the scientific evidence regarding the potential of *P. major* compared with CHX in the management of canine periodontitis. A systematic search was conducted in PubMed and Scopus (2020–2025) following PRISMA guidelines and included in vitro, in vivo, and clinical studies. *Plantago major* extracts demonstrated significant inhibition of periodontal pathogens such as *Porphyromonas gingivales*, *Fusobacterium nucleatum*, and *Streptococcus mutans*, in addition to reducing inflammatory mediators (IL-6, TNF- $\alpha$ , PGE2, IL-1 $\beta$ ), promoting wound healing in multiple animal models, and showing antimicrobial potential in nanoformulations. However, most of these studies were performed in vitro or in species other than dogs, which limits their direct clinical applicability. In contrast, clinical research in canines regarding CHX remains scarce and methodologically constrained, preventing a precise assessment of its efficacy. *Plantago major* represents a promising therapeutic alternative for veterinary periodontal health; nevertheless, well-designed, controlled clinical trials in dogs are required to directly compare its safety and efficacy with those of CHX.

**Keywords:** chlorhexidine, phytotherapy, canine periodontitis, *Plantago major*.

## Propiedades antimicrobianas, antiinflamatorias y aplicaciones clínicas de *Plantago major* como alternativa a la clorhexidina en la periodontitis canina

### RESUMEN

La periodontitis canina es una enfermedad frecuente en la práctica veterinaria, con impacto en la salud oral y sistémica. La clorhexidina (CHX) es el antiséptico estándar en protocolos periodontales; sin embargo, su uso en perros está limitado por efectos adversos y escasa evidencia clínica. *Plantago major* (*P. major*) presenta propiedades

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antimicrobianas, antiinflamatorias y cicatrizantes. El objetivo de esta revisión fue evaluar la evidencia científica sobre el potencial de *Plantago major* frente a la CHX en el manejo de la periodontitis canina. Se realizó una búsqueda sistemática en PubMed y Scopus (2020-2025) siguiendo las directrices PRISMA, que incluyó estudios *in vitro*, *in vivo* y ensayos clínicos. Los extractos de *Plantago major* mostraron inhibición significativa de patógenos periodontales como *Porphyromonas gingivales*, *Fusobacterium nucleatum*, y *Streptococcus mutans*, además de reducir mediadores inflamatorios (IL-6, TNF- $\alpha$ , PGE2, IL-1 $\beta$ ), promover cicatrización en diversos modelos animales y mostrar un potencial en nanoformulaciones con actividad antimicrobiana. Sin embargo, la mayoría de estos estudios fueron *in vitro* o en especies distintas al perro, lo que limita su aplicabilidad clínica. En contraste, la investigación clínica en caninos respecto a la CHX es escasa y metodológicamente restringida, lo que impide valorar con precisión su eficacia específica. *Plantago major* representa una alternativa terapéutica prometedora en la salud periodontal veterinaria, pero se requieren ensayos clínicos controlados en caninos que comparen su seguridad y eficacia frente a la CHX.

**Palabras clave:** clorhexidina, fitoterapia, periodontitis canina, *Plantago major*.

## INTRODUCTION

Periodontitis is among the most prevalent oral pathologies in dogs. Epidemiological studies report that more than 70% of adult dogs exhibit some degree of periodontal disease, with prevalences reaching up to 90% in geriatric individuals and small or brachycephalic breeds (Cunha et al., 2022; Santibáñez et al., 2021). This condition is characterized by a progressive inflammatory process that compromises the dental supporting tissues, leads to periodontal attachment loss, and promotes alveolar bone resorption, ultimately resulting in tooth mobility and loss (Niemiec et al., 2022).

Periodontitis originates from dysbiosis of the oral biofilm, in which commensal bacteria are replaced by pathogens such as *Porphyromonas gulae*, *Fusobacterium nucleatum* (*F. nucleatum*), and *Treponema* species. These microorganisms trigger a host inflammatory response that accelerates tissue destruction (Kwack et al., 2025; Yasuda et al., 2024). The impact is not restricted to the oral cavity, as the

infection may induce recurrent bacteremia and has been associated with systemic disorders, including renal disease, cardiac conditions, and metabolic disturbances in dogs (Heidrich et al., 2025; Wallis et al., 2024).

Chlorhexidine (CHX), at concentrations of 0.12–0.2%, is the reference antiseptic in veterinary dentistry, with proven efficacy in plaque reduction, gingivitis control, and reduction of the oral microbial load (Bellows et al., 2019). Nevertheless, despite its effectiveness, prolonged use of CHX presents important limitations. Adverse effects have been reported, including dental and mucosal staining, taste alteration, increased calculus formation, rejection due to its bitter flavor, and, more recently, the risk of inducing resistant strains or increased microbial tolerance. These constraints support the need to identify new alternatives that may complement or replace CHX in the management of canine periodontitis (Wallis et al., 2024).

Phytotherapy offers an alternative approach for the development of new

therapies in veterinary medicine. Several plant species have demonstrated antimicrobial, anti-inflammatory, and wound-healing effects in *in vitro* and *in vivo* studies. Among them, *Plantago major* (*P. major*), widely used in ethnomedicine, has gained attention due to emerging scientific evidence. This species has shown activity against oral pathogens such as *F. nucleatum*, as well as anti-inflammatory and wound-healing properties validated in oral mucosal models (Jahanimoghadam et al., 2024; Zhakipbekov et al., 2023).

Although these findings are encouraging, the available evidence still presents substantial limitations. Most studies have been conducted under *in vitro* conditions or in human subjects, with few clinical trials performed in dogs with periodontitis. In addition, variability in methodologies, concentrations, formulations, and evaluated outcomes limits the possibility of establishing consistent and comparable conclusions (Croft et al., 2022; Shin et al., 2023).

The search for phytotherapeutic alternatives to CHX in canine periodontitis has important clinical, scientific, and social implications. In veterinary practice, *Plantago major* extracts could represent complementary options with a favorable safety profile and greater acceptance among owners. From a scientific perspective, their study may promote the generation of translational evidence between human and veterinary dentistry, thereby strengthening the “One Health” approach. From a social standpoint, growing interest in natural and sustainable therapies aligns with global trends in animal and human health (Cunha et al., 2022; Memè et al., 2024).

The relevance of this topic is also associated with the need for cost-effective interventions in settings with limited access

to conventional products. The development of plant-based veterinary formulations could represent a viable alternative for public health programs and preventive campaigns in resource-restricted communities, thereby promoting animal welfare and reducing the burden of periodontal disease in canine populations (Hashim et al., 2024).

Although several studies have documented the antimicrobial and anti-inflammatory properties of *Plantago major*, no review has yet integrated the available evidence within the context of canine periodontitis or compared it with CHX. This lack of a structured synthesis limits the clinical application of these alternatives and hinders the definition of priorities for future research.

This review synthesizes and critically analyzes the scientific evidence published over the last five years regarding the use of *Plantago major* as an alternative to CHX in the prevention and treatment of canine periodontitis. Its antimicrobial and anti-inflammatory properties against periodontal pathogens and inflammatory mediators are examined, along with its applications in oral health, including biofilm inhibition, mucosal healing, and tissue regeneration, as well as the available evidence on CHX in the management of canine periodontitis.

## METHODOLOGY

A systematic search was conducted in accordance with the PRISMA 2020 guidelines, covering the phases of study identification, screening, and inclusion (Page et al., 2021). The methodological strategy was structured using the PICO model, in which the target population comprised dogs diagnosed with periodontitis,

as well as *in vitro* studies involving canine periodontopathogenic bacteria. The evaluated intervention corresponded to the use of *Plantago major* extract, whereas chlorhexidine (CHX) at concentrations between 0.12% and 0.2% served as the comparator. The analyzed outcomes included bacterial plaque reduction, gingival inflammation, probing depth, halitosis, and bacterial load, all of which are clinically and microbiologically relevant for the characterization of periodontal disease.

During the identification phase, a bibliographic search was performed in the PubMed/MEDLINE and Scopus databases using an expanded search strategy to retrieve the largest possible number of relevant scientific publications. In PubMed, the search was organized into three main thematic blocks: the first related to the intervention (*Plantago major*), the second to the condition (periodontitis or periodontal disease), and the third to the species and comparator (dogs and CHX). These blocks were combined both integratively and independently to obtain direct and indirect evidence. In Scopus, equivalent progressive combinations were applied using the same terms. All retrieved records were managed using the bibliographic software Mendeley (Elsevier), which enabled the removal of duplicate entries prior to further screening.

In the selection phase, the predefined inclusion criteria were applied: (i) *in vivo* studies in dogs with periodontitis or *in vitro* studies against canine periodontopathogenic bacteria; (ii) interventions based on *Plantago major* extracts; (iii) the presence of a comparator, preferably CHX; and (iv) reporting of clinical or microbiological outcomes. Articles published prior to 2020, studies conducted in species other than dogs without translational applicability,

anecdotal reports, brief communications, and reviews not indexed in scientific databases were excluded.

Finally, only articles that fulfilled all established criteria were included. Data extraction was performed in a systematic and independent manner. Owing to the methodological heterogeneity among the selected studies, conducting a formal systematic review was not feasible; therefore, a critical narrative review was undertaken. This approach allowed the integration of studies according to the predefined outcomes, consistently aligned with the PICO-based structure. All procedures related to the search, selection, and inclusion of studies are detailed in the adapted PRISMA 2020 flow diagram (Figure 1), which summarizes the methodological decisions adopted throughout the review.

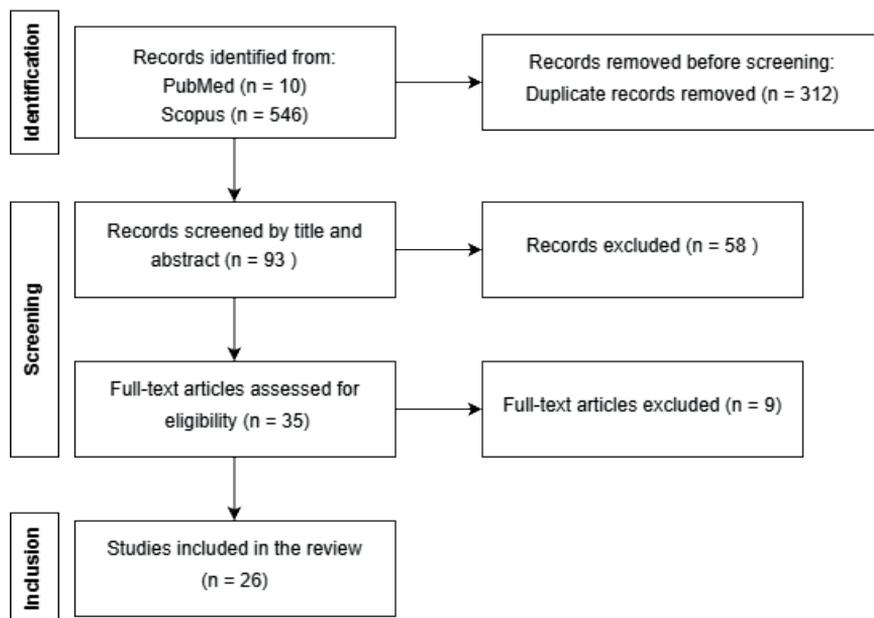
The included studies were analyzed and organized according to three predefined thematic axes: (i) the antimicrobial and anti-inflammatory properties of *Plantago major*; (ii) its applications in oral health, biofilm control, and wound-healing processes; and (iii) the use of CHX in the management of canine periodontitis.

## RESULTS AND DISCUSSION

Three types of articles were considered: *in vitro* studies ( $n = 20$ ), clinical trials ( $n = 4$ ), and complementary reviews ( $n = 2$ ). The findings derived from these studies are presented below, structured according to the analytical axes previously defined in this review.

### Antimicrobial and anti-inflammatory properties of *Plantago major*

The available evidence regarding the pharmacological properties of *Plantago major* supports its antimicrobial activity



**FIGURE 1.** PRISMA 2020 flow diagram adapted for the narrative review.

Source: adapted by the authors from The PRISMA 2020 statement: an updated guideline for reporting systematic reviews (Page et al., 2021).

against pathogenic bacteria, including antimicrobial-resistant strains. In particular, ethanolic leaf extracts produced inhibition zones of up to 22.18 mm against *Pseudomonas aeruginosa* isolated from burn wounds, in a concentration-dependent manner (Turki Monawer & Abdulkahar Mammani, 2023). Likewise, extracts prepared from dried leaves and plant residues exhibited activity against *Staphylococcus aureus* (*S. aureus*), with a minimum inhibitory concentration (MIC) of 1.25 mg/mL for strain 25,923 (Petrović et al., 2022). Similarly, methanolic extracts demonstrated bactericidal effects against methicillin-resistant *S. aureus*, reaching an MIC of 2.5 mg/mL (de Sousa et al., 2025). These findings were obtained using different extraction methods and concentrations, generating substantial methodological

variability that limits direct comparison. Therefore, although *Plantago major* exhibits antimicrobial activity, standardized and comparable protocols are required to validate its efficacy for canine oral therapy.

The antimicrobial capacity of *Plantago major* also extends to oral pathogens, and its effectiveness may be enhanced through synergistic interactions with antibiotics. In this regard, seed extracts showed efficacy against *Streptococcus mutans*, with an MIC of 1 mg/mL and a minimum bacteriostatic concentration of 2 mg/mL, producing inhibition zones of  $17.33 \pm 0.1$  mm (Mozafar et al., 2023). Moreover, a bactericidal synergistic effect was reported between methanolic extracts of *Plantago major* and imipenem against carbapenemase-producing *Klebsiella* strains, as well as a bacteriostatic effect when

combined with cephalothin and oxacillin against methicillin-resistant *S. aureus* (de Sousa et al., 2025). Although these results demonstrate a promising synergistic antimicrobial effect of *Plantago major* with antibiotics against oral pathogens, they are based exclusively on in vitro studies, which limits their clinical extrapolation. Furthermore, the lack of validation in animal models under complex oral biofilm conditions restricts their direct applicability. Thus, despite encouraging findings, the absence of in vivo studies limits the current clinical application of *Plantago major* in canine oral health.

Regarding anti-inflammatory activity, *Plantago major* is capable of modulating inflammatory mediators, achieving effects comparable to those of conventional drugs. In an in vitro study, an ethanolic extract at 0.5 mg/mL reduced prostaglandin E2 (PGE2) production in lipopolysaccharide-stimulated human monocytes, with inhibition ranging from 24.7% to 36.5%, values similar to the 26.3% observed with low-dose aspirin (Majkić et al., 2020). Complementarily, in an in vivo model of ulcerative colitis induced in rats, oral administration of leaf extracts at 700 mg/kg reduced levels of interleukin 6 (IL-6), tumor necrosis factor alpha (TNF- $\alpha$ ), PGE2, and interleukin 1 beta (IL-1 $\beta$ ) (Farid et al., 2022). Although these results support the anti-inflammatory potential of *Plantago major*, the diversity of models and extraction methods prevents direct extrapolation to clinical practice. These findings indicate that *Plantago major* has potential applicability in inflammatory processes as part of complementary therapeutic strategies.

Concerning in vivo anti-inflammatory efficacy, histological analyses have demonstrated significant reductions in

inflammatory biomarkers. In an experimental rat model of ulcerative colitis, administration of leaf extract at 700 mg/kg decreased the ulcer index and levels of IL-6, TNF- $\alpha$ , PGE2, myeloperoxidase, and malondialdehyde (Farid et al., 2022). Additionally, in a rheumatoid arthritis model, the n-hexane-insoluble fraction administered at 560 mg/kg reduced leukocyte migration to  $20.57 \pm 0.99\%$ , with effects comparable to those observed with indomethacin (Triastuti et al., 2022). In contrast, a study in women with obesity reported that *Plantago major* supplementation did not reduce TNF- $\alpha$  levels, although increases in vascular endothelial growth factor A (VEGF-A) and leptin were observed (Skrypnik et al., 2021). These variations reflect the heterogeneity of the experimental models and extract fractions evaluated. Consequently, large-scale, controlled clinical trials are required to confirm the efficacy and safety of *Plantago major* in anti-inflammatory therapies.

The anti-inflammatory and antimicrobial potential of *Plantago major* is partly attributable to its complex and rich phytochemical composition. Identified compounds include flavonoids, phenolic compounds, and triterpenes, which are considered the principal contributors to its biological activity (Majkić et al., 2020; Petrović et al., 2022). Computational simulation studies have revealed that compound NSC 86473 exhibited high affinity for cyclooxygenase-2, surpassing even celecoxib (Sunkara et al., 2023). These findings suggest that enzymatic inhibition may constitute a relevant pharmacological mechanism. However, as these results were obtained from in silico models, experimental validation is required to confirm their applicability. Therefore, computational chemistry tools

may accelerate the identification of active principles and guide the optimization of extracts for therapeutic purposes.

Beyond experimental studies, the anti-inflammatory activity of *Plantago major* has also been documented in patents related to the genus *Plantago*. One study reported that anti-inflammatory activity represents the most frequently registered application for *Plantago major* (Vendruscolo et al., 2022). This biological effect has been attributed to its metabolites, including flavonoids, terpenoids, alkaloids, fatty acids, and polysaccharides, which exhibit recognized pharmacological potential (Samuelson, 2000). Nevertheless, the lack of standardization in extraction methods, together with the limited availability of clinical trials in humans, represents a major limitation for clinical practice. Therefore, further research employing standardized extraction protocols and well-designed controlled clinical trials is required to validate the efficacy and safety of *Plantago major*.

### **Applications of *Plantago major* in oral health, biofilm control, and wound healing**

In the field of oral health, *Plantago major* has been investigated for its antimicrobial activity against biofilms and its capacity to promote wound-healing processes. The latter property has been demonstrated in several experimental models, suggesting substantial potential for application in oral regenerative processes, particularly under hyperglycemic conditions. For example, one study developed a dermal patch containing *Plantago major* extract and silver nanoparticles that enhanced epidermal reconstruction and accelerated wound healing (Kartini et al., 2021). Similarly, in a model of ulcerative colitis,

intraperitoneal administration of leaf extract at 700 mg/kg reduced the ulcer index and histopathological damage (Farid et al., 2022). In addition, the incorporation of *Plantago major* into electrospun nanofibers composed of hyaluronic acid and polyvinyl alcohol improved biomaterial fabrication processes (De Castro et al., 2022). However, most of these investigations have focused on the skin or gastrointestinal mucosa. Therefore, extrapolation to the canine oral mucosa requires the development of specific pharmaceutical formulations and validation in appropriate experimental models. Overall, this evidence supports the wound-healing potential of *Plantago major*; however, its application in the canine oral cavity still requires targeted studies.

Within the context of periodontal health, enzymatic inhibition is particularly relevant because several enzymes participate in connective tissue degradation. In this regard, the aqueous extract of the aerial parts of *Plantago major* subsp. *major* inhibited hyaluronidase activity by 27.04% and collagenase activity by 21.92%, whereas calceorioside B achieved even greater inhibition, reaching 41.16% at a concentration of 100 µg/mL (Genc et al., 2020). The modulation of these enzymes suggests potential periodontal tissue protection and reinforces the therapeutic potential of *Plantago major*. Nevertheless, the efficacy and bioavailability of these compounds in the canine oral environment have not been confirmed; therefore, clinical application remains challenging. Consequently, *Plantago major* could be considered an additive in veterinary oral care products, provided that adequate clinical validation is achieved.

Innovative applications of *Plantago major* include nanoformulations that enhance its antimicrobial effect in oral biofilm control.

In this context, silver nanoparticles synthesized using ethanolic leaf extracts exhibited inhibitory activity against *S. aureus* ( $7.31 \pm 0.532$  mm) and *Escherichia coli* ( $8.59 \pm 0.222$  mm) at a concentration of 20  $\mu\text{g/mL}$  (Sukweenadhi et al., 2021). Notably, the extract alone showed no antimicrobial effect, indicating a synergistic interaction with the nanoparticles. However, direct evaluations against oral biofilms, assessments of activity against canine periodontal pathogens, and investigations of long-term toxicity and safety in the oral environment are still lacking. Therefore, nanoformulations containing *Plantago major* represent a promising strategy but require specific validation in canine oral biofilms and comprehensive safety studies.

Traditionally, *Plantago major* has been used in oral health products, particularly in toothpaste formulations, because of its anti-inflammatory and antimicrobial activity. References to “llantén” are often generic and lack specification of species or concentration, which limits reproducibility (Vendruscolo et al., 2022). Nevertheless, the scientific literature confirms a diverse bioactive profile, including inhibition of oral pathogens (Mozafar et al., 2023; Pesantes-Sangay et al., 2020), stimulation of wound healing (Kartini et al., 2021), and enzymatic inhibition in periodontal tissues (Genc et al., 2020). Despite these findings, the absence of in vivo canine studies and the heterogeneity of the extracts employed restrict clinical applicability. Accordingly, well-designed clinical trials in dogs are required to define safety, efficacy, and formulation parameters for the treatment of periodontitis and other oral lesions.

A major research gap in the oral application of *Plantago major* is the lack of canine models. Most studies have been conducted in vitro against human

pathogens, such as *Porphyromonas gingivalis* and *Fusobacterium nucleatum*, or in rats with cutaneous wounds or ulcerative colitis (Farid et al., 2022; Kartini et al., 2021; Pesantes-Sangay et al., 2020). Furthermore, in vivo studies analyzing oral biofilms are unavailable, despite the fact that their structural resistance may limit the efficacy observed against planktonic bacteria (Bouali et al., 2024; Mozafar et al., 2023). These limitations hinder extrapolation because of interspecies differences in microbiota composition, oral physiology, and wound-healing processes. Thus, the absence of canine models and oral biofilm studies represents a critical validation gap for *Plantago major* in canine oral health.

Another critical aspect is the limited optimization of extracts and formulations. In many cases, high concentrations or solvents such as ethanol are used without conducting safety or palatability assessments for oral products. Similarly, wound-healing effects have been evaluated in skin and gastrointestinal mucosa (Farid et al., 2022; Kartini et al., 2021), but not in oral mucosa, which exhibits distinct healing characteristics. These limitations underscore the need to improve methodologies and technologies related to safety, formulation, and clinical application in the oral cavity. Consequently, the development of appropriate pharmaceutical formulations and targeted studies in canine models is required to confirm the effectiveness and safety profile of *Plantago major*.

### Use of chlorhexidine in canine periodontitis

To integrate the information on the properties of *Plantago major* and to contrast it with chlorhexidine (CHX) in the context of canine periodontitis, Table 1 was prepared. This table summarizes their main

**TABLE 1.** Comparison of key aspects between *Plantago major* and chlorhexidine in the management of canine periodontitis

Aspect	<i>Plantago major</i>	Chlorhexidine (CHX)	Clinical implications	References
Chemical composition and bioactive compounds	Flavonoids, phenolic compounds, iridoids, phenylethanoid glycosides, fatty acids, terpenoids, alkaloids, and polysaccharides.	Synthetic antiseptic; not considered a botanical extract with a phytochemical profile.	<i>Plantago major</i> contains metabolites with antimicrobial, anti-inflammatory, and wound-healing effects; CHX is characterized by its direct antimicrobial action.	De Castro <i>et al.</i> , 2022; De Sousa <i>et al.</i> , 2025; Gawor <i>et al.</i> , 2022; Majkić <i>et al.</i> , 2020; Petrović <i>et al.</i> , 2022; Triastuti <i>et al.</i> , 2022
Anti-inflammatory activity	Reduces edema and leukocyte migration; decreases IL-6, TNF- $\alpha$ , PGE2, and COX-2 in colitis models and oral epithelial cells.	No relevant anti-inflammatory effect reported; its primary role is antimicrobial.	<i>Plantago major</i> may act as an adjuvant in periodontitis control by improving the therapeutic response.	Farid <i>et al.</i> , 2022; Genc <i>et al.</i> , 2020; Sunkara <i>et al.</i> , 2023; Triastuti <i>et al.</i> , 2022
Wound healing	Accelerates oral wound healing in rats; improves closure of burns and cutaneous wounds; inhibits hyaluronidase and collagenase.	Mainly used for post-surgical antiseptics; not a specific wound-healing promoter.	<i>Plantago major</i> may enhance periodontal repair and tissue recovery beyond antiseptics alone.	De Castro <i>et al.</i> , 2022; Farid <i>et al.</i> , 2022; Genc <i>et al.</i> , 2020; Jahanimoghadam, Javidan, Ranjbar, Torabi, Kakoei, <i>et al.</i> , 2024; Sukweenadhi <i>et al.</i> , 2021
Considerations in canine periodontitis	In vitro activity against <i>Porphyromonas gingivalis</i> and <i>Fusobacterium nucleatum</i> ; nanoparticles synthesized with <i>Plantago major</i> active against <i>S. epidermidis</i> and <i>S. aureus</i> .	Broad-spectrum antimicrobial; commonly used in dogs as a 0.12% CHX rinse for postoperative care and plaque/gingivitis control.	<i>Plantago major</i> represents a multimodal adjuvant alternative (antimicrobial + anti-inflammatory + wound healing) and may complement or partially substitute CHX.	Avanti <i>et al.</i> , 2024; Gawor <i>et al.</i> , 2022; Pesantes-Sangay <i>et al.</i> , 2020

Source: own elaboration.

phytochemical characteristics, biological effects, limitations, and clinical relevance.

The comparison presented in Table 1 highlights the antimicrobial, anti-inflammatory, and wound-healing properties of *Plantago major*. Nevertheless, CHX remains the reference antimicrobial agent against periodontal pathogens, underscoring the need for studies that validate the potential of *Plantago major* as a complementary or alternative option in the management of canine periodontitis.

Regarding the clinical use of CHX in oral practice, its application is limited and is usually described as part of postoperative protocols rather than being evaluated as an isolated intervention. In this context, one study employed a 0.12% CHX rinse after open periodontal therapy and reported improvements in clinical signs. However, the absence of a control group and the small sample size ( $n = 9$ ) hinder attribution of the effects exclusively to CHX and limit the generalizability of the findings (Gawor et al., 2022). Furthermore, no studies directly comparing CHX with placebo or topical alternatives in dogs with periodontal disease are currently available. Consequently, further investigations with greater methodological rigor and larger sample sizes are required to support its clinical effectiveness and safety.

More broadly, CHX is widely recognized as the “gold standard” in periodontal therapy because of its antimicrobial efficacy. This status is supported mainly by in vitro studies demonstrating its activity against periodontal pathogens. For instance, a formulation containing 0.12% CHX combined with 0.05% cetylpyridinium chloride produced inhibition zones of up to 24.9 mm against *Porphyromonas gingivalis* and *Fusobacterium nucleatum* (Pesantes-Sangay et al., 2020), whereas

CHX alone achieved a 24 mm inhibition zone against *Streptococcus mutans* (Mozafar et al., 2023). Although these results confirm its antimicrobial potential, they are derived from in vitro models that do not fully represent the complexity of the canine oral biofilm. Nevertheless, they reinforce the role of CHX as a key antimicrobial agent in canine periodontitis.

Despite its recognized efficacy, the clinical use of CHX is limited by adverse effects, including dental and lingual staining, and the potential development of bacterial resistance (Pesantes-Sangay et al., 2020). Under these circumstances, compounds such as *Plantago major* may act as adjuncts or even substitutes in therapeutic protocols for the management of canine periodontitis (Petrović et al., 2022). These limitations justify the search for natural alternatives that provide comparable and safe antimicrobial effects. Accordingly, *Plantago major* emerges as a potential alternative for the treatment of canine periodontitis, even though CHX continues to represent the current therapeutic standard.

## CONCLUSIONS

The available evidence supports the potential of *Plantago major* as an antimicrobial and anti-inflammatory agent against periodontal pathogens and key inflammatory mediators. However, the heterogeneity of experimental designs and the lack of clinical trials in dogs limit its direct applicability in veterinary practice.

In addition, *Plantago major* has demonstrated beneficial effects on wound-healing processes and on the inhibition of degradative enzymes, particularly when incorporated into emerging technologies such as nanoparticles and bioactive

dressings. Nevertheless, the scarcity of studies in specific oral models and the lack of formulations adapted for veterinary use limit its therapeutic implementation.

Although CHX remains the reference standard in the postoperative management of canine periodontitis, the limited evidence, characterized by small sample sizes and the absence of adequate control groups, prevents robust conclusions regarding its isolated effects. This methodological gap underscores the need to explore alternatives such as *Plantago major* in well-designed comparative studies, with the potential to diversify and optimize therapeutic protocols in veterinary periodontal health.

### CONFLICT OF INTEREST

The authors declare that there were no conflicts of interest in the preparation of this review.

### FUNDING SOURCES

The authors declare that no funding sources were received for the preparation of this review.

### USE OF ARTIFICIAL INTELLIGENCE

The authors declare that no artificial intelligence tools were used in the preparation of this review article.

### ETHICS COMMITTEE

This article is a literature review and did not involve experiments with animals or humans; therefore, approval from an institutional ethics committee was not required.

### ACKNOWLEDGMENTS

The authors thank the Doctoral Program in Health Sciences, Graduate School, Universidad Nacional del Altiplano, Puno.

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### Forma de citación del artículo:

Epezua, O. H. & Padilla-Caceres, T.C. (2026). Antimicrobial, anti-inflammatory properties and clinical applications of *Plantago major* as an alternative to Chlorhexidine in canine periodontitis. *Rev. Med. Vet. Zoot.* 73(1): e123135. <https://doi.org/10.15446/rfmvz.v73n1.123135>