

Plant-Based Antibacterial Strategies Against *Porphyromonas gingivalis*: A Systematic Review

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Porphyromonas gingivalis is an anaerobic Gram-negative coccus known to play a significant role in periodontal disease. Although tetracycline is a potent antibiotic with excellent antibacterial activity against this organism, it should be used judiciously owing to its side effects and the possibility of antibiotic resistance. In the search for alternate treatment strategies against *P.gingivalis*, herbal products show sufficient promise. Therefore, we performed a scoping review to understand our current knowledge on the efficacy of herbal extracts against *P.gingivalis*. Using specific keywords, databases like PubMed, Medline, Lilacs, Web of science, and Scopus were searched for in vitro studies reporting the efficacy of various herbal products against *Porphyromonas gingivalis*. After screening and elimination of irrelevant and duplicate articles, 94 articles were included in this review. Data was extracted from these articles, and the findings are summarised. Numerous herbal extracts have been evaluated for their efficacy against *P.gingivalis*. Extracts from coffee beans, *Moringa oleifera* leaves and *Allium sativum* pods were effective at low concentrations. *Artemisia herba-alba* showed a maximum zone of inhibition against the organism. Our literature search and review suggest that a wide range of herbal extracts have been evaluated for their effectiveness against *P.gingivalis*. However, a majority of such extracts have never been evaluated in more than one study, and some do not have proper positive and negative controls, prompting us to view their results with extreme caution. Further research in the form of animal studies and clinical trials is essential to identify and develop a potent alternative to tetracycline for use in periodontal disease management.

Keywords: Antibacterial activity; Herbal extract; Inhibition zone diameter; Minimum inhibitory concentration; *Porphyromonas gingivalis*.

Porphyromonas gingivalis is an anaerobic Gram-negative coccus which plays a key role in the initiation and progression of periodontal disease.

This microbe invades epithelial tissue and modifies the host defence by chemokine paralysis (inhibiting secretion of IL-8). It also possesses a battery of

enzymes like collagenase and gingipains that adds to its virulence.¹ This cannot be eliminated from the periodontal pocket by mechanical debridement alone (scaling and root planing) as they can invade the periodontal tissue. Use of antimicrobials has become an important part of anti-infective therapy in the management of periodontal disease. The antibiotic of choice used here is tetracycline which has good antibacterial efficacy and anti-collagenase activity. Side effects of the drug (like nausea, headache, stomach upset) and emergence of antimicrobial resistant microbe are vital factors to be considered in their usage.²

In recent years herbal alternatives are being researched for management of diseases. These products have bioactive compounds that

could be used in anti-infective therapy against *P.gingivalis*.³ In this review we have analysed the existing data on the antibacterial efficacy of herbal extracts against *P.gingivalis* to find a promising alternative to antibiotics in the management of periodontal disease.

MATERIALS AND METHODS

This systematic review was prospectively registered with the Open Science Framework (OSF.IO/H8K43). A comprehensive literature search was conducted across PubMed, MEDLINE, Web of Science, and Scopus databases using the keywords “Plant extract”, “Herbal extract”, AND “*Porphyromonas gingivalis*”. Articles published up

Table 1. Quantitative synthesis of published studies evaluating plant-based antimicrobials against oral pathogens (n = 115)

Domain	Parameter	Value
Study characteristics	Total studies ⁴⁻⁶	115
	Publication period	1993–2024
	Studies per decade	1990s-3; 2000s-9; 2010s-49; 2020 to 2024-54
Outcome measures	Studies reporting MIC/MBC	96 (83.5%)
	Studies reporting IZD	52 (45.2%)
	Studies reporting both	33 (28.7%)
	Studies reporting neither	6 (5.2%)
Plant material	Most studied plant part	Leaves (57; 49.6%)
	Second most studied part	Fruits (21; 18.3%)
	Bark / stem bark	14 (12.2%)
	Seeds / galls / gum / resin	13 (11.3%)
	Rhizome / tuber	7 (6.1%)
	Part not specified	18 (15.7%)
Extraction method	Ethanol-based extracts	46 (40.0%)
	Aqueous / water-based	24 (20.9%)
	Methanol	18 (15.7%)
	Dichloromethane	9 (7.8%)
	Acetone	8 (7.0%)
	Non-polar solvents (hexane, chloroform)	7 (6.1%)
	Solvent not specified	14 (12.2%)
Antimicrobial potency	MIC range reported	0.13 – 55,000 µg/mL
	Studies reporting MIC d”100 µg/mL	38 (33.0%)
	Studies reporting MIC >1,000 µg/mL	29 (25.2%)
Comparators (IZD studies)	Any positive control used	46 / 52 (88.5%)
	Chlorhexidine (0.12–0.2%)	27 (51.9%)
	Antibiotic controls (any)	19 (36.5%)
	No control stated	6 (11.5%)
Reporting quality indicators	Unit-standardized MIC values	72 (62.6%)
	Multiple plants per study	29 (25.2%)
	Multiple solvents per study	21 (18.3%)

to and including 30th June 2024 were considered for inclusion.

Inclusion criteria

- In vitro studies specifically evaluating crude plant extracts against *Porphyromonas gingivalis*
- Studies reporting quantitative antimicrobial endpoints: minimum inhibitory concentration (MIC) and/or inhibition zone diameter (IZD) using

agar diffusion methods

- Primary research articles published in peer-reviewed journals

Exclusion criteria

- Studies evaluating commercially available herbal products or formulations
- Research on combined extracts from multiple plant species

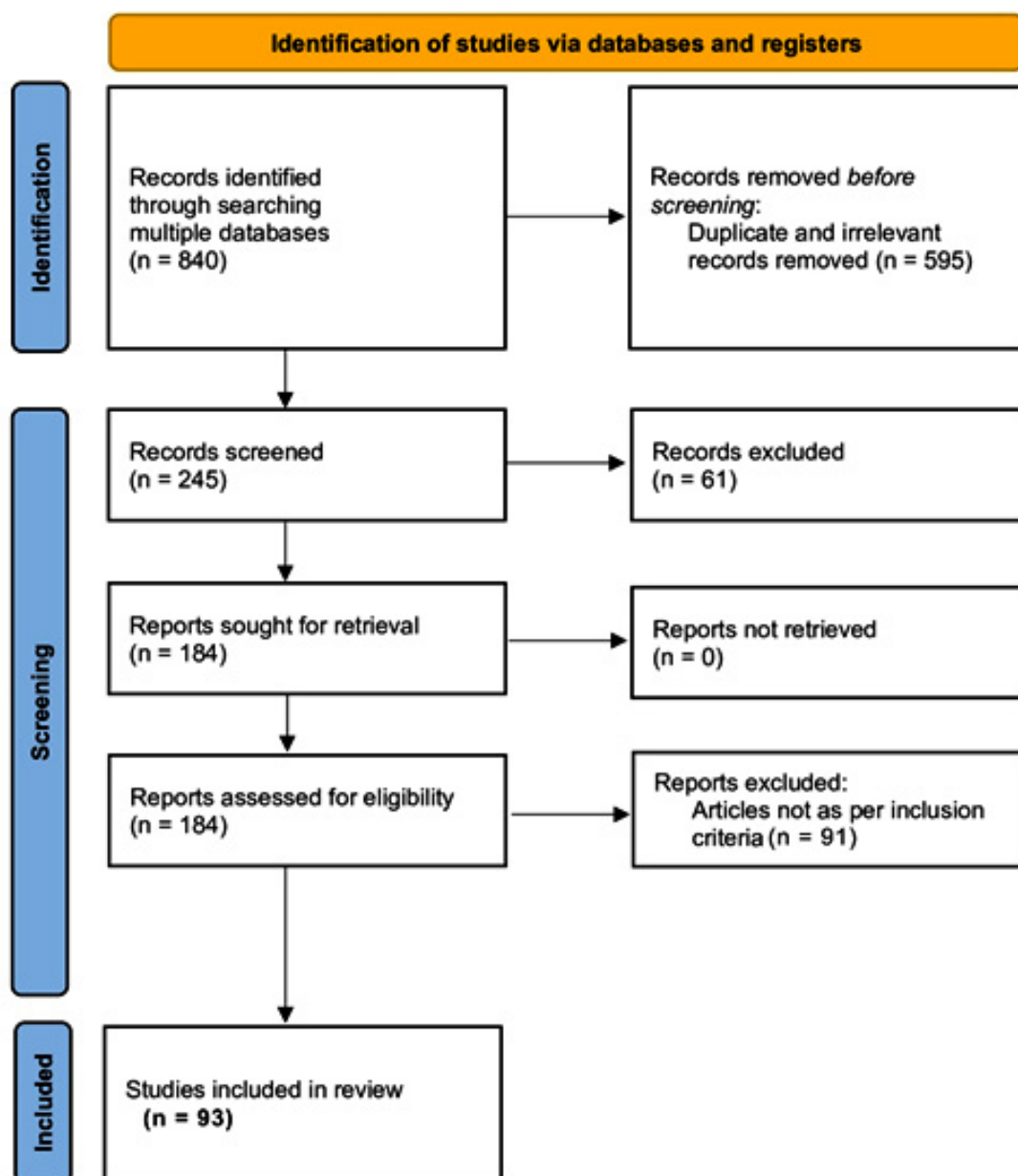


Fig. 1. PRISMA-SCR Flowchart

- Investigations of isolated chemical compounds or purified phytochemicals from plant extracts
- Clinical studies, animal studies, or reviews/meta-analyses
- Studies lacking specific quantitative MIC or IZD data against *P. gingivalis*

From 823 identified records, articles were independently screened by two reviewers (Authors

1 and 5) following PRISMA-SCR guidelines. After title/abstract screening, full-text assessment, and resolution of discrepancies by consensus discussion, 88 studies met all inclusion criteria and were included in the qualitative synthesis (selection flowchart: Fig-1).

RESULTS

The summary of the data extracted is tabulated (Table 1). The research for antibacterial activity of plant extract against *Porphyromonas gingivalis* started by Clark *et al.* in 1993 using *Acacia senegal* (arabica gum).⁴ Studies have been conducted on plants native to Brazil, China, India, Sudan and United States of America. There has been a lot of research on this domain but there are very few repetitions. It can be observed that five studies were conducted on *Punica granatum*

Table 2. Year-wise distribution of the published studies

Year	Number of studies
1997 to 2000	4 ⁴⁻⁷
2001 to 2005	3 ⁸⁻¹⁰
2006 to 2010	4 ¹¹⁻¹⁴
2011 to 2015	24 ¹⁵⁻³⁸
2016 to 2020	29 ³⁹⁻⁶⁷
2021 to 2025	29 ⁶⁸⁻⁹⁶

Table 3. Commonly researched plants

Plant studied	Author	MIC (in µgm/ml)	IZD (in mm)
<i>Punica granatum</i> L. (Pomegranate)	Rosas-Pinon <i>et al.</i> ²¹	125	—
	Veloso <i>et al.</i> ⁶⁴	170	3.0/ ±/ 0.0
	Abullais <i>et al.</i> ⁶⁹	5210	14 ± 0.45
	Ghafar and Dahham, ⁷⁸	—	41
	Madhloom AF, ⁷⁷	6.25 mg/ml	14.02
<i>Pistacia lentiscus</i> (Mastic gum/ fruit)	Sterer N ¹¹	—	10.5-13.7
	Karygianni <i>et al.</i> ²⁹	20	—
	Koychev <i>et al.</i> ⁴⁷	—	25
	Carrol <i>et al.</i> ⁶¹	64(Woody part)	—
	Carrol <i>et al.</i> ⁶¹	8 (Fruit)	—
<i>Azadirachta indica</i> (Neem)	Heyman <i>et al.</i> ⁴⁴	10 iM	—
	Carrol DH <i>et al.</i> ⁶¹	64	—
	Saqui <i>et al.</i> ⁶⁹	640	13 ± 0.36
	Müller-Heupt LK <i>et al.</i> ⁷²	256 (Acetone)	—
	Müller-Heupt LK <i>et al.</i> ⁷²	1024 (70% Ethanol)	—

Table 4. Plant extracts with the least minimum inhibitory concentration (MIC)

Plant	Part	MIC (µgm/mL)	Author
<i>Coffea canephora</i>	Bean	0.2	Bharath <i>et al.</i> ³⁸
<i>Moringa oleifera</i>	Leaf	0.8	Ida MJ <i>et al.</i> ⁸⁴
<i>Allium sativum</i>	Pods	1.21±0.37	Alirezai <i>et al.</i> ⁵⁵
<i>Rheum palmatum</i>	Root	4	Müller-Heupt <i>et al.</i> ⁷²
<i>Lycium barbarum</i>	Fruit	6.25	Sanghavi AD <i>et al.</i> ⁷¹
<i>Copaifera reticulata</i>	Oleoresin	6.25	Bardaji DK <i>et al.</i> ⁴²

µgm/mL- microgram per millilitre

Table 5. Plant extracts with the highest inhibition zone diameter in agar diffusion test

Plant	Inhibition diameter (mm)	Author
<i>Artemisia herba-alba</i>	49.00 ± 0.82	Arbia <i>et al.</i> ⁴⁵
<i>Opuntia ficus-indica</i>	48.83 ± 1.03	Arbia <i>et al.</i> ⁴⁵
<i>Camellia sinensis</i>	42.00 ± 0.41	Arbia <i>et al.</i> ⁴⁵
<i>Ocimum sanctum</i>	33.79 ± 1.82	Jayanti <i>et al.</i> ⁴⁸
<i>Camellia sinensis</i>	26.65±1.56	Araghizadeh <i>et al.</i> ²³

L. (Pomegranate) and four studies on *Pistacia lentiscus* (fruit or mastic gum) and *Azadirachta indica* (Neem). Minimum inhibitory concentration data reveal that green coffee bean extract has the least value of 0.2 µgm/mL by Bharath N *et al.*,³⁸ followed by leaves of *Moringa oleifera* (Drumstick tree) with 0.8µgm/mL by Ida MJ *et al.*,⁸⁴ and pods of *Allium sativum* with 1.2 µgm/mL by Alirezaei S *et al.*⁵⁵ The results of agar disc diffusion method showed that *Artemisia herba-alba* (white wormwood) has the maximum inhibition diameter of 49 mm by Arbia L *et al.*⁴

DISCUSSION

Porphyromonas gingivalis, the primary focus of this review, belongs to Socransky's "red complex"—a highly pathogenic complex comprising *P. gingivalis*, *Tannerella forsythia*, and *Treponema denticola*, that strongly correlates with deep periodontal pockets (>6 mm), attachment loss, and bleeding on probing.⁹⁷ These species form synergistic biofilms characterized by proteolytic activity, nutrient sharing, and immune evasion, driving dysbiosis from health-associated communities toward tissue-destructive inflammation. Recent metagenomic analyses confirm red-complex enrichment in severe periodontitis, alongside orange-complex species (*Campylobacter rectus*, *Fusobacterium nucleatum*) and emerging pathogens like *Parvimonas micra* and *Filifactor alocis*.

Sonets *et al.* applied whole-genome shotgun metagenomics to mild vs. severe cases, revealing that red-complex dominance, coupled with specific metabolic pathways (like amino acid degradation) and network interactions, predicts disease progression.⁹⁸ Non-microbial

factors, including cardiovascular comorbidities and recent antibiotic exposure, further amplified severity signatures, underscoring periodontitis as a polymicrobial, multifactorial disorder rather than a monopathogen infection.

P. gingivalis acts as a keystone pathogen, using gingipains, fimbriae, and outer membrane vesicles to orchestrate community virulence and host immune dysregulation, despite low abundance.⁹⁷ Plant extracts targeting *P. gingivalis* may thus indirectly modulate broader dysbiotic consortia, aligning with Ecological plaque hypotheses.

The investigation of plant extracts for antibacterial activity against *Porphyromonas gingivalis* began in the early 1990s. For more than a decade, the number of publications in this field remained relatively limited. However, a marked increase in research output has been observed after 2010. This surge in interest may be attributed to growing concerns regarding the adverse effects associated with conventional antimicrobials and the escalating problem of antibiotic resistance in periodontal pathogens. A detailed year wise distribution of published studies is provided in Table 2.

The studies included in this review investigated a wide variety of plant extracts, with only a limited number of repetitions across different herbs. Interestingly, in cases where the same plant was evaluated by multiple authors, the results often showed notable variability in both minimum inhibitory concentration (MIC) values and inhibition zone diameters. These discrepancies may be explained by differences in the plant part utilized for extraction, the choice of solvent, or variations in extraction methodology.

For example, Carrol *et al.* in 2020 reported

that *Pistacia lentiscus* demonstrated an MIC of 8 µg/mL when an ethanolic extract of the fruit was tested, compared with 32 µg/mL when the woody portion of the plant was used and 64 µg/mL when water served as the extraction solvent.⁶¹ Similarly, Gawade *et al.* in 2025 observed pronounced variability in *Sphaeranthus indicus*, where the MIC for leaf extract was 12.5 µg/mL, whereas the flower extract yielded an MIC as high as 100 µg/mL.⁹⁶

These variations highlight the importance of standardizing extraction protocols in phytochemical and antimicrobial research. Since MIC is defined as the lowest concentration of an antimicrobial agent that completely inhibits the visible growth of a microorganism after incubation, even modest methodological differences can significantly influence reported outcomes.

Furthermore, such inconsistencies emphasize the critical need for quality control and reproducibility standards in the development of herbal-based therapeutic agents. Establishing uniform guidelines for plant part selection, extraction solvent, and preparation methods would not only enhance comparability across studies but also strengthen the translational potential of promising plant extracts for clinical applications. A summary of the most frequently investigated plant extracts, along with their MIC values and inhibition diameters, is presented in Table 3.

The reported MIC values of commonly used antimicrobials against *Porphyromonas gingivalis* are 0.4 µg/mL for chlorhexidine,⁴³ 0.016 µg/mL for tetracycline,¹⁰ and 0.313 µg/mL for doxycycline.³⁰ Analysis of the extracted data (Table 4) demonstrates that among the plant-derived preparations, *Moringa oleifera* leaves exhibited the lowest MIC at 0.8 µg/mL.⁸⁴ This value is of particular relevance as it is comparable to the inhibitory range of some standard antimicrobial agents currently used in clinical practice. Importantly, these findings suggest that selected plant extracts, particularly *Moringa oleifera*, may serve as promising adjuncts or potential alternatives to conventional antimicrobials in the management of periodontal infections, especially in the context of increasing antibiotic resistance. A consolidated list of the plant extracts demonstrating the lowest MIC values against *P. gingivalis* is presented in Table 4.

The inhibition zone diameter (IZD) is

defined as the maximum linear distance across the clear zone of microbial growth inhibition surrounding a test compound in the agar diffusion assay. In several studies, plant extracts demonstrated IZDs that were comparable to, and in some cases exceeded, those of standard antimicrobial agents. For example, extracts have produced inhibition zones within the range of 32.25–40 mm, which is similar to the activity observed with doxycycline (32.25–40 mm),³⁹ while others achieved IZDs between 16–33.5 mm,²⁹ comparable to 0.2% chlorhexidine.

These results highlight the potential of certain plant extracts to provide inhibitory effects against *P. gingivalis* comparable to conventional antimicrobials. Nonetheless, the variability in outcomes across studies emphasizes the importance of methodological standardization to validate these findings. The plant extracts demonstrating the highest inhibition zone diameters are summarized in Table 5.

Conceptualizing periodontitis as a “continuum”, with antecedents (genetic/systemic risks), triggers (dysbiosis), mediators (inflammation/oxidative stress), and outcomes, demands multimodal therapies beyond mechanical debridement alone. Benahmed *et al.* advocated integrating biofilm control with host modulation, locally delivered antimicrobials, probiotics/prebiotics for microbiome reshaping, and nanoparticle drug delivery to target matrix metalloproteinases and cytokines.⁹⁹

Emerging antimicrobials exemplify this shift. Tolentino *et al.* tested cannabidiol (CBD) against a 33-species subgingival biofilm model, finding 500–1000 µg/mL CBD significantly reduced total biomass and red-complex proportions (*P. gingivalis*, *T. forsythia*). This was comparable to 0.12% chlorhexidine, while relatively enriching green-complex health-associated species. CBD’s efficacy was greatest when applied pre-biofilm formation (post-debridement mimicry), suggesting ecological rebalancing over broad suppression, though clinical trials remain needed.¹⁰⁰

Recent work in this platform has found that *Camellia sinensis* polyphenols inhibited gingipain activity, a key virulence factor of *P. gingivalis*.¹⁰¹ The modulation of inflammatory cytokines and reduced ROS production by *Moringa oleifera* extracts was also observed. These factors

strengthen the mechanistic insights and the pharmacological rationale for incorporating these botanicals as adjuncts in periodontal therapy.^{102,103}

Emerging molecular studies have also shed light on the mechanisms of action underlying plant-derived antibacterial activity. Wu *et al.* investigated dihydrochalcone flavonoids such as phloretin and phlorizin, showing these compounds cause morphological disruption, increase membrane permeability, and induce apoptosis in *P. gingivalis*.¹⁰⁴ Transcriptomic profiling revealed interference with DNA function and oxidative stress pathways, supporting phytochemicals as multi-target agents capable of disrupting bacterial survival and resistance mechanisms.

These frameworks contextualize the plant extracts reviewed here as adjuncts within continuum-based care. Extracts matching chlorhexidine/doxycycline MICs (e.g., *Moringa oleifera* 0.8 µg/mL, *Coffea canephora* 0.2 µg/mL) or the ones with anti-gingipain activity could integrate with strategies like antimicrobial photodynamic therapy, host modulation (e.g., via polyphenols inhibiting gingipains/NF- κ B), or microbiome-targeted probiotics. Future studies should evaluate phytochemicals against multi-species biofilms, clinical isolates across red/orange complexes, and systemic inflammatory markers to validate their role in precision periodontal management.

In terms of clinical relevance, mouthwash formulations containing *Punica granatum L.* have undergone randomized clinical trials, confirming comparable or superior efficacy to chlorhexidine in reducing gingival inflammation and plaque indices.¹⁰¹ Despite modest in vitro activity against *P. gingivalis* measured by some studies, the clinical benefits likely stem from synergistic anti-inflammatory and antimicrobial effects of multiple phytochemicals such as punicalagin and quercetin, which inhibit key virulence enzymes of *P. gingivalis*.

Limitations of Existing Studies

Although numerous studies have investigated the antibacterial activity of plant extracts against *Porphyromonas gingivalis*, several limitations were evident. First, many studies did not incorporate appropriate positive controls (such as chlorhexidine, doxycycline, or tetracycline). The absence of controls undermines the reliability,

comparability, and overall significance of the reported findings. Second, the majority of the research was conducted using laboratory stock strains, particularly ATCC 33277, with relatively few studies evaluating other strains such as W381, W50, or W83. Only a limited number utilized clinical isolates, which are more representative of pathogens encountered in patients.

Notably, differences in strain type influenced reported antimicrobial activity. For example, Mendes *et al.* in 2020 found that fractions of *Salvia officinalis* demonstrated an MIC of 50 µg/mL against ATCC 33277, but a higher MIC of 100 µg/mL against clinical isolates.⁶² Similarly, *Allium sativum* aqueous extract showed remarkable variation, with an MIC of 1.2 µg/mL against ATCC 33277,⁵⁵ compared with 4.4 mg/mL against the W50 strain.⁹³ Nakao *et al.* in 2024 reported comparable discrepancies for *Camellia sinensis* extracts, with MIC values of 250 µg/mL for ATCC 33277 and W50, but a significantly lower 125 µg/mL for the W83 strain.⁹² These findings highlight that MIC values are highly strain-dependent, and reliance solely on stock cultures may not accurately reflect clinical efficacy.

Therefore, to improve translational relevance, future research should prioritize standardized methodologies, inclusion of appropriate positive controls, and testing across multiple strains, particularly clinical isolates. Such measures will enhance the reproducibility and clinical applicability of plant-derived antibacterial agents in periodontal therapy.

Future research should focus on standardizing extraction methodologies, incorporating appropriate positive controls, and testing across multiple *P. gingivalis* strains, particularly clinical isolates. In addition, mechanistic studies, toxicity assessments, and clinical trials are essential to validate efficacy and ensure the translational potential of plant-derived extracts as safe and sustainable adjuncts in periodontal therapy.

CONCLUSION

The potential of plant-derived compounds as alternatives to conventional therapies has garnered significant attention within the medical

field. To effectively transition these botanical extracts into clinical practice, comprehensive in vitro characterization and subsequent human trials are imperative. Antibacterial properties are particularly crucial for addressing periodontal diseases, such as those caused by *P. gingivalis*. This review underscores the diverse array of plant species investigated globally for their antimicrobial efficacy against this pathogen. While certain plant extracts have demonstrated comparable antibacterial activity to existing antimicrobial agents, further research is warranted to isolate the specific phytochemicals responsible for these effects and to explore their potential for drug development.

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This research did not involve human participants, animal subjects, or any material that requires ethical approval.

Informed Consent Statement

This study did not involve human participants, and therefore, informed consent was not required

Clinical Trial Registration

This research does not involve any clinical trials.

Permission to reproduce material from other sources

Not applicable

Author contributions

Nitya Kala: Conceptualization, Methodology, Data Collection, Analysis, Writing – Original Draft; Ravi Sarayan: Conceptualization, Methodology, Supervision; Dorairaj Jayachandran:

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