ORAL SPHERE
JOURNAL OF DENTAL AND HEALTH SCIENCES

Oral Sphere Journal of Dental and Health Sciences

www.oralsphere.com ISSN: 3049-2904 (Online) , 3107-6262 (Print)

Review Article

Periodontal Vaccines: Boon or Mere Promise in Modern Dentistry?

Chhavi Khanna [1], Anchal Sood [1], Swantika Chaudhry [1], Harsukhman Kaur[1], Ankita Nayyar[1], Gurdev Chopra[2]

[1] Department of Periodontology & Oral Implantology, Baba Jaswant Singh Dental College, Hospital & Research Institute, Ludhiana, Baba Farid University of Health Sciences, Ludhiana, Punjab, India

[2] Private Practitioner, Dr Tarsem's Life Cure Hospital, Bhikiwind, Punjab, India

Citation: Khanna C, Sood A, Chaudhry S, Kaur H, Nayyar A, Chopra G. Periodontal Vaccines: Boon or Mere Promise in Modern Dentistry?. Oral Sphere J. Dent. Health Sci. 2026;2(1):57-62

For reprints contact:
publisher@fontfusionspublication.com

Received: September 29, 2025;
Revised: October 25, 2025;
Accepted: December 06, 2025;
Published: January 01, 2026

***Corresponding author:** Chhavi Khanna
Email: Khannachhavi563@gmail.com

DOI: https://doi.org/10.63150/osjdhs.2026.10

ABSTRACT

Periodontal disease is a chronic inflammatory disorder resulting from the dynamic interplay of pathogenic bacteria within the oral microbiota and host defense, ultimately leading to alveolar bone loss, tooth mobility, and tooth exfoliation. Conventional periodontal treatments (mechanical debridement and adjunctive antimicrobial agents) essentially control established disease, without offering lifelong protective immunity against relevant periodontopathogens. Periodontal vaccination is a new immunotherapeutic approach for inducing the host to generate an immune response toward certain bacterial virulence factors so that colonization and tissue destruction of periodontopathic bacteria in hosts are inhibited. Diverse kinds of vaccines, such as whole cell, subunit, recombinant protein, DNA and conjugate vaccines have been studied for their potential to elicit humoral and cellular immune responses. Preclinical trials in animal models have shown some positive outcomes, including reduction of bacterial load, inhibition of alveolar bone loss, and systemic as well as mucosal immune responses. Gingipain subunit and fimbrial Porphyromonas gingivalis DNA vaccines have provided particularly encouraging results. However, limitations such as the polymicrobial nature of periodontitis, interindividual differences in immune responses, safety issues and lack of human clinical trials still exist. These limitations can be potentially overcome by focusing on the mucosal Sdelivery systems, nanoparticle-based vaccines, multivalent formulations and personalized immunotherapy in future studies. Periodontal vaccination is a novel concept of preventive dentistry, which shifts the current treatment model to prophylactic methods based on immune-mediated disease prevention and life-long maintenance of periodontal as well as overall health.

Keywords: Alveolar bone loss, DNA vaccine, Periodontitis, Subunit vaccine, Vaccination

BACKGROUND:

Periodontal disease is a prevalent chronic oral condition affecting millions of people worldwide and is responsible for substantial tooth loss, functional disability and reduced quality of life [1]. It is a multi-factorial inflammatory disease mostly derived from the intricate interaction of pathogenic bacteria within dental biofilm and the host immune response [2]. Although these traditional periodontal therapies, which include scaling and root planing, surgical approaches and the use of adjuvant antimicrobials, are highly effective in controlling disease progression, they are essentially aimed at modulating existing disease rather (and not before it occurs) than preventing its onset at an immunologic level [3]. This limitation has fueled investigation of alternative strategies, with undoubtedly the use of periodontal vaccines as one of the most interesting alternatives [4].

Dental vaccine is one of the novel preventive approaches towards the reduction or elimination of microbial pathogens that cause periodontal diseases [5]. These vaccines, in contrast to traditional treatment modalities, are intended to pre-prune the immune system of its ability to recognize and neutralize specific periodontal pathogens before they have a chance to colonize the oral cavity and induce damaging immuno-inflammatory pathways [6]. This strategy may not only be applicable for preventing further disease progression, but also to direct periodontal care more toward long-term prevention, which is in line with the current philosophy of dentistry [7].

The basis for a periodontal vaccine is derived from recognition of the fact that certain bacteria, predominantly Porphyromonas gingivalis, *Aggregatibacter actinomycetemcomitans* and *Tannerella forsythia*, are key players in the onset and development of periodontitis [8]. These organisms have a battery of virulence factors, including lipopolysaccharides, fimbriae and proteolytic enzymes, that lead to host immune response with tissue damage and osteolysis [9]. Vaccine approaches aim at targeting these virulence factors, thereby abating their pathogenesis and lessening the degree of host-mediated tissue injury. Utilising our body's own adaptive immune system, they provide a preemptive solution to controlling periodontal pathogens that antibiotics and mechanical debridement alone fail to deliver [10].

A number of preclinical studies have shown promise for periodontal vaccines with respect to antibody responses. as well as tissue destruction in the animals. These include whole-cell vaccines, subunit vaccines, recombinant protein-based vaccines and DNA-based vaccines; all with their own sets of advantages and disadvantages [11]. The aim is to generate a protective immune response able to convey long-term protection against colonization of important periodontopathogens. While the majority of such vaccine strategies are still at a pre-clinical or early experimental stage, they offer an exciting opportunity to alter how periodontal disease could be treated in the future [12].

The advantage of periodontal vaccination is not limited to the scope of individual oral health. Since periodontitis has become associated with systemic diseases such as cardiovascular disease, Diabetes Mellitus or adverse pregnancy outcomes, an effective periodontal vaccine might also help decrease the systemic inflammatory load [13]. This wider impact serves to emphasize the interdisciplinary significance of such advances for both dental and general medicine or public health. Despite all this promise, many obstacles still face this approach, which include heterogeneity in patients' immune response; polymicrobial etiopathogenesis of PD and requirements for long-term clinical trials to establish efficacy as well as safety [14]. However, periodontal vaccine is still in its infancy, but it has the potential to change the paradigm of preventive dentistry [15].

Accordingly, the present review seeks to summarize the development of periodontal vaccination from its scientific basis to recent improvements and challenges ahead, as well as pointing out where we are heading in the future.

REVIEW:

Historical Perspective on Periodontal Vaccines:

The idea of using vaccines in periodontology dates back to the early 20th century, when crude bacterial extracts were tested. However, these lacked specificity and safety. Modern biotechnology and molecular immunology have enabled the development of targeted vaccines that can stimulate precise immune responses against defined antigens. [16].

Pathogenesis of Periodontal Disease and Rationale for Vaccination:

An imbalance in the oral microbiome, with a prevalence of pathogenic bacteria, is responsible for periodontal

disease, which causes tissue destruction mediated by the host. Of these, Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans and Tannerella forsythia are classified as keystone pathogens [17].

These include the excretion of virulence factors by said bacteria:

And lipopolysaccharides (LPS) – all elicit robust inflammatory reactions.

Gingipains (proteolytic enzymes from P. gingivalis) – chew up host proteins and immune factors.

Fimbriae – Adhesin Factors that enable adhesion and invasion of bacteria [18].

Types of Periodontal Vaccines

1. Whole-Cell Vaccines

- Contain inactivated or attenuated periodontopathogens.
- Provide broad antigenic stimulation but risk unwanted immune responses.
- Early studies with *A. actinomycetemcomitans* showed antibody production, but efficacy was limited.

2. Subunit Vaccines

- Use purified antigens (fimbriae, LPS, gingipains).
- More specific and safer compared to whole-cell vaccines.
- Example: Fimbrial protein-based vaccines against *P. gingivalis*.

3. Recombinant Protein Vaccines

- Genetic engineering allows the production of specific proteins in bacterial or yeast systems.
- Example: Recombinant gingipain fragments as antigens.

4. DNA Vaccines

- Use plasmids encoding bacterial antigens.
- Host cells produce antigens and stimulate humoral and cellular immunity.
- Example: DNA vaccine encoding *P. gingivalis* fimbriae.

5. Conjugate Vaccines

- Combine polysaccharide antigens with carrier proteins.
- Aim to improve immunogenicity of weak antigens [19].

Types of Periodontal Vaccines are shown in Table 1

Table 1: Types of Periodontal Vaccines and Their Characteristics

Vaccine Type	Description	Examples
Whole-Cell Vaccines	Contain inactivated or attenuated periodontopathogens; provide broad antigenic stimulation, but may trigger unwanted immune responses.	Early studies with *Aggregatibacter actinomycetemcomitans* showed antibody production, but efficacy was limited.
Subunit Vaccines	Use purified antigens such as fimbriae, lipopolysaccharides (LPS), or gingipains; safer and more specific than whole-cell vaccines.	Fimbrial protein-based vaccines against *Porphyromonas gingivalis*.
Recombinant Protein Vaccines	Produced through genetic engineering in bacterial or yeast systems to generate specific antigens.	Recombinant gingipain fragments from *P. gingivalis*.
DNA Vaccines	Plasmids encoding bacterial antigens introduced into host cells stimulate both humoral and cellular immunity.	DNA vaccine encoding *P. gingivalis* fimbriae.
Conjugate Vaccines	Polysaccharide antigens combined with carrier proteins to enhance the immunogenicity of weak antigens.	Still experimental in periodontal applications.

Mechanisms of Action of Periodontal Vaccines:

Whole-cell vaccines work by acting as a potent nonspecific immune stimulant by presenting numerous bacterial antigens to the host's defense system. They are easy to produce, although they are not very specific and can induce hypersensitivity [20].

Subunit vaccines work by targeting and inactivation specific virulence proteins (e.g., lipopolysaccharides, fimbriae, proteolytic enzymes). Their main benefit includes safety and specificity, but their coverage is limited to a small number of pathogens [21].

Subunit vaccines, such as the recombinant-protein vaccines, are generated through genetic engineering to activate both humoral and cellular immune responses. Such vaccines provide strong specificity for specific antigens, but their preparation is intricate and expensive, discouraging massive utilization [22].

DNA vaccines function by the entry of plasmids, including bacterial antigens, into host cells. This in turn produces antigen within the host and provokes long-term T- and B-cell mediated immunity. They are assumed to be stable and robust; however, their clinical confirmation is limited [23].

Conjugate vaccines increase the immunogenicity of poor antigens like polysaccharides in bacteriaby conjugating them with carrier proteins. They have shown systemic efficacy, but only an experimental and investigational role for periodontics is justified at the present stage of knowledge [24].

Mechanisms of Action of Periodontal Vaccines are shown in Table 2.

Table 2: Mechanisms of Action of Periodontal Vaccines

Vaccine Type	Mechanism of Action	Advantages	Limitations
Whole-cell vaccine	Broad immune stimulation via multiple antigens	Simple to prepare	Risk of hypersensitivity, non-specific
Subunit vaccine	Neutralizes specific virulence factors	Safe, targeted	Limited coverage of pathogens
Recombinant protein vaccine	Stimulates humoral and cellular immunity	High specificity	High production cost
DNA vaccine	Induces long-term immunity (both T-cell and B-cell)	Stable, durable	Limited clinical validation
Conjugate vaccine	Enhances weak antigen immunogenicity	Effective in systemic use	Still experimental in periodontics

DISCUSSION

The research on periodontal vaccines has largely advanced in the pre-clinical phase through experimental studies. Animal studies have shed light, demonstrating that immunization with Porphyromonas gingivalis antigens resulted in a marked reduction of alveolar bone loss and bacterial load in the periodontal tissue. Such studies clearly indicate the possibility of vaccination to control periodontal devastation [25].

Subunit vaccines against specific virulence factors, for example, gingipains from P. gingivalis, have shown promising results in inducing antibody-mediated protection. These antibodies have the potential to neutralize proteases and reduce tissue degradation [26].

DNA vaccines also offer hope, as these have been demonstrated to induce systemic and mucosal immunity in experimental murine models. Such a double activation of immunity is important for periodontal protection, affording long-term protection both at the local oral site and in the systemic circulation [27].

These results demonstrated the possibility to developing periodontal vaccines, but clinical studies in humans are rare. The bulk of the evidence is so far limited to laboratory and animal studies. Nevertheless, preclinical information suggests that this concept is efficacious and there is a strong rationale for translation to the human setting, with safety and efficacy grounds as well as delivery issues needing resolution [28].

There are important clinic advantages in such a periodontal vaccine development. Their prophylactic efficacy consists of the prevention of periodontitis development by initiating a protective response of the host immune system against important pathogens. As adjuvant treatment, vaccination may decrease the need for repeated mechanical- or surgical-based treatments and thereby facilitate better long-term control of disease [29].

Crucially, periodontal vaccination has systemic health implications since periodontitis is related to systemic diseases (cardiovascular disease, diabetes mellitus, and adverse pregnancy outcomes). Vaccines may potentially and in part reduce the systemic inflammatory load, thus favoring general health [30].

As far a health economic point of view, vaccination option might be a cost-effective policy. The prevention of the initial onset or recurrence of periodontitis would lower this demand for continual periodontal therapy and thus contribute to diminished long-term cost both for patients and health-care providers [31].

LIMITATION

However, there still exist great challenges in translating periodontal vaccines into the clinic. The polymicrobial aetiology of periodontitis has made vaccine development difficult, as it is caused by a consortium of bacterial species rather than one pathogen. Moreover, genetic and immune diversity at the individual level could explain distinct vaccine efficacy in diverse populations [32].

Safety issues also pose a major hurdle, such as the fact that large doses of DNA vaccines may trigger autoimmune or hypersensitivity reactions. In addition, there is a wide translational gap, and few clinical trials involving humans have been conducted to confirm findings from preclinical studies. Because of this paucity of clinical evidence, vaccines have not been widely accepted as a routine therapy for the treatment of periodontitis [33].

Last but not least, one should add that very high regulatory barriers must be faced before dental vaccines can be accepted in clinical practice. Comprehensive safety testing, long-term efficacy trials and consensus on international standards of care are all needed along the way [34].

FUTURE AIMS AND SCOPE

The future of periodontal vaccination lies in innovation and personalization. Mucosal vaccines, administered via nasal or oral sprays, present a non-invasive delivery method that could improve patient compliance and provide effective local immunity in the oral cavity. Nanoparticle-based vaccine systems are being explored to enhance antigen stability and targeted delivery, ensuring a stronger and more reliable immune response [35].

Another promising direction is the development of multivalent vaccines, which can simultaneously target multiple periodontopathogens, thereby addressing the polymicrobial nature of periodontitis. In addition, personalised immunotherapy, guided by an individual's oral microbiome profile and genetic predisposition, may offer tailored preventive and therapeutic solutions [36].

With these advancements, periodontal vaccines hold the potential not only to control periodontal disease but also to contribute significantly to systemic health promotion.

CONCLUSION

Looking ahead, innovations such as mucosal delivery systems, nanoparticle-based vaccines, and multivalent formulations are expected to overcome existing limitations, making periodontal vaccination a viable, long-term solution for periodontal disease prevention. Personalized immunotherapy, based on an individual's genetic and oral microbiome profile, could further enhance the specificity and efficacy of these vaccines. With continued research and well-designed clinical trials, periodontal vaccines could transform the landscape of periodontal care, shifting the focus from treatment to true prevention, ultimately benefiting not just oral health but also systemic well-being.

REFERENCES

1. Hashim NT et al. Int J Environ Res Public Health. 2025 Apr 16;22(4):624. [DOI: 10.3390/ijerph22040624]
2. Petersen PE et al. Periodontol 2000. 2012 Oct;60(1):15-39. [DOI: 10.1111/j.1600-0757.2011.00425.x]
3. Tariq M et al. Int J Pharm Investig. 2012 Jul;2(3):106-22. [DOI: 10.4103/2230-973X.104394]
4. Patel P et al. Cureus. 2025 Mar 15;17(3):e80636. [DOI: 10.7759/cureus.80636]
5. Vaernewyck V et al. Front Immunol. 2021 Dec 2;12:768397. [DOI: 10.3389/fimmu.2021.768397]
6. Kudyar N et al. J Indian Soc Periodontol. 2011 Apr;15(2):115-20. [DOI: 10.4103/0972-124X.84378]
7. Janakiram C et al. Periodontol 2000. 2020 Oct;84(1):202-214. [DOI: 10.1111/prd.12337]
8. Sharma DC et al. Expert Rev Vaccines. 2007 Aug;6(4):579-90. [DOI: 10.1586/14760584.6.4.579]
9. Bertani B et al. EcoSal Plus. 2018 Aug;8(1):10.1128/ecosalplus.ESP-0001-2018. [DOI: 10.1128/ecosalplus.ESP-0001-2018]
10. Brazzoli M et al. Hum Vaccin Immunother. 2023 Aug 1;19(2):2228669. [DOI: 10.1080/21645515.2023.2228669]
11. Vinayaka AM. J Dent Panacea. 2024;6(1):20-25. [DOI: 10.18231/j.jdp.2024.006]
12. Ebersole JL et al. Periodontol 2000. 2013 Jun;62(1):163-202. [DOI:10.1111/prd.12005]
13. Nazir MA. Int J Health Sci (Qassim). 2017 Apr-Jun;11(2):72-80. [PMID: 28539867]
14. Etminan S et al. Front Med (Lausanne). 2025 Jul 17;12:1619845. [DOI: 10.3389/fmed.2025.1619845]
15. S. Aadil Ahamed et al. Research J. Pharm. and Tech. 2016; 9(7):972-976. [DOI: 10.5958/0974-360X.2016.00186.4]
16. Choi JI et al. J Periodontal Implant Sci. 2010 Aug;40(4):153-63. [DOI: 10.5051/jpis.2010.40.4.153]
17. Hu W et al. J Adv Res. 2025 Jul;73:443-458. [DOI: 10.1016/j.jare.2024.08.019]
18. Jia L et al. Front Cell Infect Microbiol. 2019 Jul 18;9:262. [DOI: 10.3389/fcimb.2019.00262]
19. Malhotra Ranjan et al. Indian Journal of Dental Research 22(5): p 698-705, Sep–Oct 2011. [DOI: 10.4103/0970-9290.93459]
20. Laupèze B et al. NPJ Vaccines. 2021 Jul 27;6(1):93. [DOI: 10.1038/s41541-021-00354-z]
21. Hou Y et al. Acta Pharm Sin B. 2023 Aug;13(8):3321-3338. [DOI: 10.1016/j.apsb.2023.01.006. Epub 2023 Jan 10]
22. Wang M et al. Bioengineered. 2016 Apr;7(3):155-65. [DOI: 10.1080/21655979.2016.1191707].
23. Khan KH. Germs. 2013 Mar 1;3(1):26-35. [DOI: 10.11599/germs.2013.1034]
24. Rappuoli R et al. Proc Natl Acad Sci U S A. 2019 Jan 2;116(1):14-16. [DOI: 10.1073/pnas.1819612116]
25. Dhingra K et al. J Periodontol. 2010 Nov;81(11):1529-46. [DOI: 10.1902/jop.2010.100138]
26. Yonezawa H et al. Infect Immun. 2001 May;69(5):2858-64. [DOI: 10.1128/IAI.69.5.2858-2864.2001]
27. Su F et al. Hum Vaccin Immunother. 2016 Apr 2;12(4):1070-9. [DOI: 10.1080/21645515.2015.1114195]
28. Fal Dessai et al. International Journal Of Drug Research And Dental Science, 5(3), 1-10. [DOI: 10.36437/ijdrd.2023.5.3.A]
29. Pattanshetty et al. Journal of Multidisciplinary Dental Research.2018:4(1);48-55. [Available from: https://jmdr-idea.com/articles/periodontal-vaccine-a-review]
30. Jain P et al. Pharmaceutics. 2021 Jul 30;13(8):1175. [DOI: 10.3390/pharmaceutics13081175]
31. Cancan Huang et al. EngMedicine, Volume 2, Issue 1, March 2025, 100052 [DOI: 10.1016/j.engmed.2024.100052]
32. Liao L et al. Int Immunopharmacol. 2024 Oct 25;140:112650. Epub 2024 Jul 29. Erratum in: Int Immunopharmacol. 2025 Aug 28;161:115093. [DOI: 10.1016/j.intimp.2024.112650].

33. Olivieri B et al. Vaccines (Basel). 2021 Jul 22;9(8):815. [DOI: 10.3390/vaccines9080815]
34. Săndulescu O et al. Germs. 2023 Jun 30;13(2):104-107. [DOI: 10.18683/germs.2023.1373]
35. Yusuf H et al. Hum Vaccin Immunother. 2017 Jan 2;13(1):34-45. [DOI: 10.1080/21645515.2016.1239668]. Epub 2016 Dec 9.
36. Loeurng V et al. Vaccines (Basel). 2024 Jul 8;12(7):754. [DOI: 10.3390/vaccines12070754]

Ethical Approval: Institutional Review Board approval was not required.

Declaration of Patient Consent: Patient consent was not required as there are no patients in this study.

Financial Support and Sponsorship: Nil

Conflicts of Interest: The authors declare that they have no conflicts of interest.

Use of Artificial Intelligence (AI) - Assisted Technology for Manuscript Preparation: The authors confirm that no artificial intelligence (AI)- assisted technology was used to assist in the writing or editing of the manuscript, and no images were manipulated using AI tools.

AUTHOR CONTRIBUTIONS:

Chhavi Khanna: Corresponding author, contributed to the conceptualization, writing, and review of the manuscript.

Anchal Sood: Contributed to the literature review, data analysis, and manuscript writing.

Swantika Chaudhry: Assisted in data analysis, interpretation, and manuscript preparation.

Harsukhman Kaur: Contributed to manuscript revision and editing.

Ankita Nayyar: Assisted with literature review and manuscript writing.

Gurdev Chopra: Contributed to the clinical perspective and manuscript revision.

ABBREVIATIONS USED IN THE STUDY:

a) **LPS**: Lipopolysaccharides
b) **P. gingivalis**: *Porphyromonas gingivalis*
c) **A. actinomycetemcomitans**: *Aggregatibacter actinomycetemcomitans*
d) **T. forsythia**: *Tannerella forsythia*
e) **DNA**: Deoxyribonucleic Acid

DECLARATION ON PUBLICATION ETHICS:

The authors declare that they adhere to the COPE guidelines on publishing ethics, as described elsewhere at https://publicationethics.org/. The authors also undertake that they are not associated with any other third party (governmental or non-governmental agencies) linking with any form of unethical issues related to this publication. The authors also declare that they are not withholding any information that is misleading to the publisher regarding this article.

DECLARATION ON OFFICIAL E-MAIL:

The corresponding author declares that a lifetime official e-mail from their institution is not available for all authors.

COMMENTS FROM READERS:

Articles published in the ORAL SPHERE JOURNAL OF DENTAL AND HEALTH SCIENCES are open for relevant post-publication comments and criticisms, which will be published immediately, linking to the original article without open access charges. Comments should be concise, coherent, and critical in fewer than 1000 words.

DISCLAIMER:

The Oral Sphere Journal of Dental and Health Sciences provides a platform for the scholarly communication of data and information to create knowledge in the dental and medical domains after adequate peer/editorial reviews and editing, with entertaining revisions where required. The views and opinions expressed are those of the author(s) and do not reflect the views or opinions of Oral Sphere Journal of Dental and Health Sciences (and/or) its publisher, Font Fusions Publication Pvt. Ltd. Font Fusions Publication remains neutral and allows authors to specify their address and affiliation details, including territory where required.