IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 24, Issue 8 Ser. 1 (August. 2025), PP 17-24
www.iosrjournals.org

Smart Shots: Current Advances In Immunization-Based Caries Control

Andria Dsouza[1], Kiran Kumar N[2], Savitha B Naik[3], Biji Brigit[4], Seema Merwade[5] Vaishnavi Kashim[6], Ansha Jasmin S[7]

[1](Resident, Department Of Conservative Dentistry And Endodontics, Government Dental College And Research Institute, Rajiv Gandhi University Of Health Sciences, Bangalore, Karnataka, India)
[2](HOD & Professor, Department Of Conservative Dentistry And Endodontics, Government Dental College And Research Institute, Rajiv Gandhi University Of Health Sciences, Bangalore, Karnataka, India)
[3](Assosciate Professor, Department Of Conservative Dentistry And Endodontics, Government Dental College And Research Institute, Rajiv Gandhi University Of Health Sciences, Bangalore, Karnataka, India)
[4](Assosciate Professor, Department Of Conservative Dentistry And Endodontics, Government Dental College And Research Institute, Rajiv Gandhi University Of Health Sciences, Bangalore, Karnataka, India)
[5](Assosciate Professor, Department Of Conservative Dentistry And Endodontics, Government Dental College And Research Institute, Rajiv Gandhi University Of Health Sciences, Bangalore, Karnataka, India)
[6](Resident, Department Of Conservative Dentistry And Endodontics, Government Dental College And Research Institute, Rajiv Gandhi University Of Health Sciences, Bangalore, Karnataka, India)
[7](Resident, Department Of Conservative Dentistry And Endodontics, Government Dental College And Research Institute, Rajiv Gandhi University Of Health Sciences, Bangalore, Karnataka, India)

Abstract:
Dental caries remains one of the most prevalent chronic diseases worldwide, particularly affecting children and underserved populations. Despite being largely preventable, caries continues to impose a significant burden on public health systems and individual well-being. Traditional strategies—such as fluoride use, dietary counseling, and oral hygiene—have had measurable success but rely heavily on long-term behavioral compliance and regular access to care. As a result, the development of a dental caries vaccine has garnered considerable interest as a more sustainable, immunologically driven solution. This review explores the pathogenesis of caries, focusing on the role of Streptococcus mutans and its key virulence factors, including glucosyltransferases, glucan-binding proteins, and antigen I/II. It outlines the immunological rationale for vaccine design, emphasizing the importance of mucosal immunity and secretory IgA. Various antigen targets, delivery platforms—including DNA, nanoparticle, and subunit vaccines—and routes of administration are examined. The manuscript also reviews clinical trial progress, highlights current challenges, and discusses adjunct strategies such as probiotics and replacement therapy. While no vaccine has yet reached the market, emerging technologies and deeper understanding of oral immunology offer hope for future breakthroughs. A successful vaccine would represent a major advancement in global oral health, especially for high-risk and resource-limited populations.

Keywords: *Dental caries, vaccine, Streptococcus mutans, mucosal immunity, secretory IgA, glucosyltransferase, nanoparticle vaccine, oral microbiome.*

Date of Submission: 23-07-2025 Date of Acceptance: 03-08-2025

I. Introduction

Dental caries remains the most widespread chronic infectious disease globally, affecting people of all ages.[1] Despite the preventive efforts such as fluoride application, oral hygiene promotion, and dietary counseling, caries continues to pose a significant public health challenge.[2] According to the Global Burden of Disease Study, billions of individuals are affected by untreated caries, with particularly high prevalence in children, underscoring both the clinical and socioeconomic impact of this condition.[3]

Caries is a complex biofilm-mediated disease driven by dysbiosis of the oral microbiome. S*treptococcus mutans*, a key cariogenic bacterium, plays a central role in initiating and sustaining the acidic environment that leads to enamel demineralization.[4] While conventional preventive measures can control the disease to some extent, they often require continuous behavioral compliance, regular access to care, and public health infrastructure, which are not equally available in all parts of the world.[5]

These limitations have spurred interest in developing a dental caries vaccine, a preventive tool that could offer long-term, population-level immunity, particularly in vulnerable pediatric populations. Over the past few

decades, researchers have explored various immunological approaches targeting *S. mutans* virulence factors, aiming to disrupt colonization, reduce acid production, or prevent biofilm formation.[6]

This review aims to synthesize current knowledge on the immunopathogenesis of dental caries, the status of vaccine development, and the diverse strategies under investigation, from protein subunit and DNA vaccines to innovative platforms like nanoparticles and mRNA-based delivery. The present review seeks to highlight the scientific progress and the practical and ethical considerations shaping the future of caries immunoprevention.

II. Etiopathogenesis Of Dental Caries

Dental caries is a multifactorial disease resulting from the dynamic interplay between microbial activity, host susceptibility, dietary habits, and time. The pathogenesis lies in the microbial shift within the dental biofilm,a structured matrix consisting of bacteria and extracellular polysaccharides that adheres to the tooth surface. Among the many organisms that colonize the oral cavity, *S. mutans* is specifically implicated in caries by virtue of its ability to ferment dietary sugars and produce acid from the fermentation product, withstand low pH, and adhere to enamel.

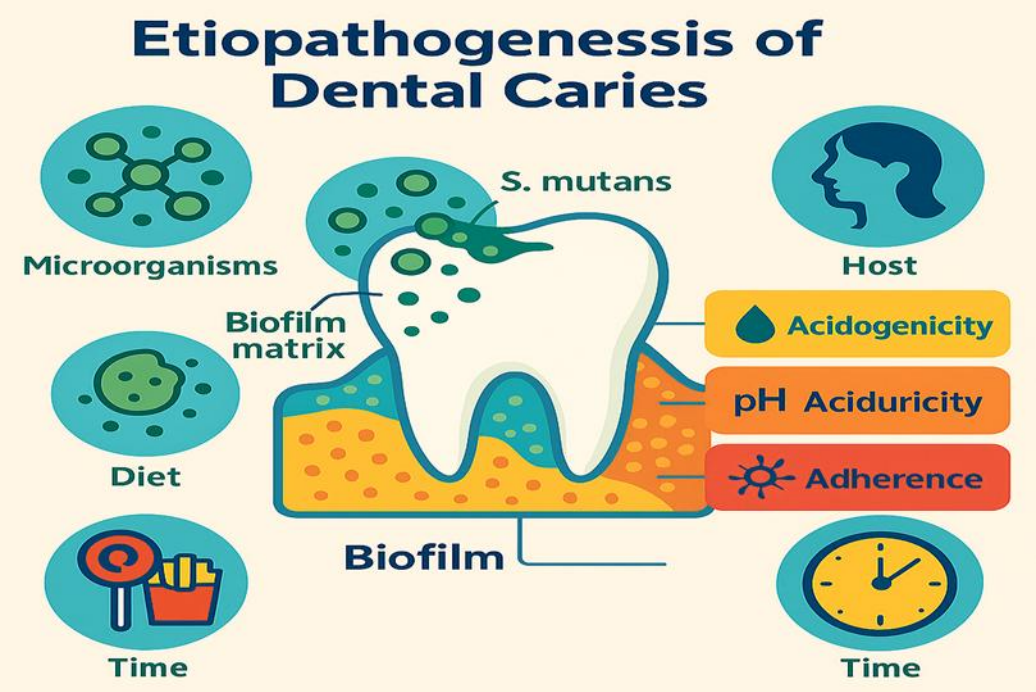

Figure 1: Etiopathogenesis of Dental caries

The virulence of *S. mutans* is associated with three main factors: acidogenicity (acid production), aciduricity (acid tolerance), and adherence.These are related to surface-associated proteins,like glucosyltransferases (GTFs), glucan-binding proteins (GBPs), and protein antigen I/II (ted as PAc). GTFs produce extracellular glucans from sucrose that create the sticky matrix to anchor the bacteria on the tooth surface and support the development of a cariogenic biofilm. In addition, PAc I/II is involved with the initial adherence to the tooth by binding to the salivary glycoproteins and dental pellicle.

The initiation and progression of caries depend on microbial factors, host, and environmental influences. Salivary flow, buffering capacity, enamel composition, and dietary patterns, especially frequent consumption of fermentable carbohydrates, can tip the balance of the oral ecosystem toward demineralization. Moreover, repeated acid attacks over time surpass the remineralization capacity of saliva and fluoride, eventually leading to cavitation.[7,8]

Understanding *S. mutans* -host interaction helps guide vaccine development by identifying targets to prevent colonization and protect oral health.

III. Immunological Basis For A Caries Vaccine

The rationale for caries vaccine stems from the recognition that *S.mutans* colonization and biofilm formation can be interrupted by stimulating protective immune responses, particularly at mucosal surfaces. The effective protection hinges on the induction of secretory immunoglobulin A (sIgA), the predominant antibody isotype in saliva that plays a key role in immune exclusion.[9]

sIgA can neutralize bacterial adhesins, block the synthesis of extracellular glucans, and interfere with the aggregation and colonization of *S. mutans*.[10] Animal studies have consistently shown that mucosal immunization can lead to the production of antigen-specific sIgA in saliva, which correlates with reduced bacterial colonization and caries development. Additionally, systemic immunity, primarily through serum IgG, may contribute to overall protection by enhancing phagocytic clearance and reducing bacterial invasion in deeper tissues.[11-13]

The"window of infectivity" generally occurs between 19 and 31 months of age, when *S. mutans* first colonizes the oral cavity.[14] Vaccination within this window could block bacterial adherence and the initial establishment of cariogenic biofilm, thereby establishing long-term protection. This is a strategy consistent with other pediatric vaccines that intended to create immunity before naturally occurring pathogens.[9]

Both cell-mediated and humoral immune responses are part of the immune protection following vaccination.[15] Antigens such as PAc, GTFs, and GBPs can elicit a T-helper response, which can support B cell activation and antibody production. However, achieving strong and lasting mucosal immunity is difficult because it requires targeted delivery methods and safe adjuvants that can activate oral lymphoid tissue without causing inflammation or side effects.[16]

IV. Vaccine Antigen Targets

Developing an effective vaccine against dental caries requires an understanding of the virulence mechanisms of *S. mutans* and the identification of molecular targets that may inhibit its ability to initiate and sustain infection. Many surface-associated proteins have been identified over the past few decades as promising antigens because of their essential functions in bacterial adhesion, biofilm formation, and acid production. PAc, GTFs, and GBPs are the most studied and well-validated antigens.[11]

Protein Antigen c (PAc)

PAc (also known as antigen I/II) is a surface fibrillar protein known to be responsible for the initial adhesion of *S. mutans* to dental pellicle by interacting with salivary agglutinin. It is comprised of two functional domains: an alanine-rich segment or A-region and a proline-rich segment (P-region), both of which are important for binding activity.[17] Immunization with PAc can stimulate specific antibodies that can block this interaction with salivary agglutinin, reducing the colonization of *S. mutans* on tooth surfaces. Despite its immunogenic potential, native PAc by itself is only a modest immunogen and therefore, must be used with effective adjuvants or utilized as a fusion protein in engineered recombinant forms.[18]

Glucosyltransferases (GTFs)

GTFs are secreted enzymes that catalyze the synthesis of extracellular glucans from sucrose. These glucans mediate bacterial adhesion to the enamel surface, and create a scaffolding for other oral microorganisms, providing stability for the plaque and enhancing its cariogenicity. Antibodies against GTFs can block the activity of the enzyme, and disrupt glucan synthesis, which would compromise biofilm structure, while reducing bacterial load as well as the acidogenic potential of the plaque.[19]

Glucan-Binding Proteins (GBPs)

GBPs bind glucans produced by GTFs and contribute to stabilizing the extracellular matrix of dental plaque. GBPs mediate cells to surfaces and cells to cells interactions, strengthening biofilm integrity. Immunological targeting of GBPs has been shown to hinder plaque development and lessen caries incidence in animal studies. Even though GBPs are less potent on their than the GTFs or PAc, they have potential synergistic effects when included in multi-component vaccines along with GTFs or Pac.[20,21]

Novel Antigens

In addition to traditional antigens, several new antigens are currently being investigated to increase vaccine efficacy. One of them includes gcrR-deficient strains of *S. mutans* that have reduced acidogenicity, making this strain viable as a replacement therapy and to inhibit wild-type strains via competitive inhibition.[22,23] Other proteins under investigation include fimbrial adhesins, flagellins (i.e., TLR5 agonists), and recombinant fusion proteins that have both antigenic and adjuvanticity functions. These antigens represent a shift towards multivalent and multi-functional-based vaccines capable of inducing strong mucosal and systemic immune responses.[24,25]

Collectively, these antigenic strategies emphasize the complex biology of *S. mutans* and the desirable vaccine-induced immune responses capable of preventing the key steps of the caries process, from initial attachment to mature biofilm development. Thus, the selection of antigens for use in an anticaries vaccine is critical to ensuring vaccine efficacy and long-lasting protection.[11]

V. Vaccine Platforms

The pursuit of an effective vaccine for dental caries development has led to the use of various vaccine platforms, each with advantages and disadvantages for delivering the antigens and eliciting strong mucosal and systemic immune responses. The goal is to achieve these immune responses safely for long-term preventative use, given the challenges posed by the oral environment. These considerations highlight the importance of technology selection for vaccine platforms.Figure 1 summarizes the various vaccine platforms available for dental caries vaccines.

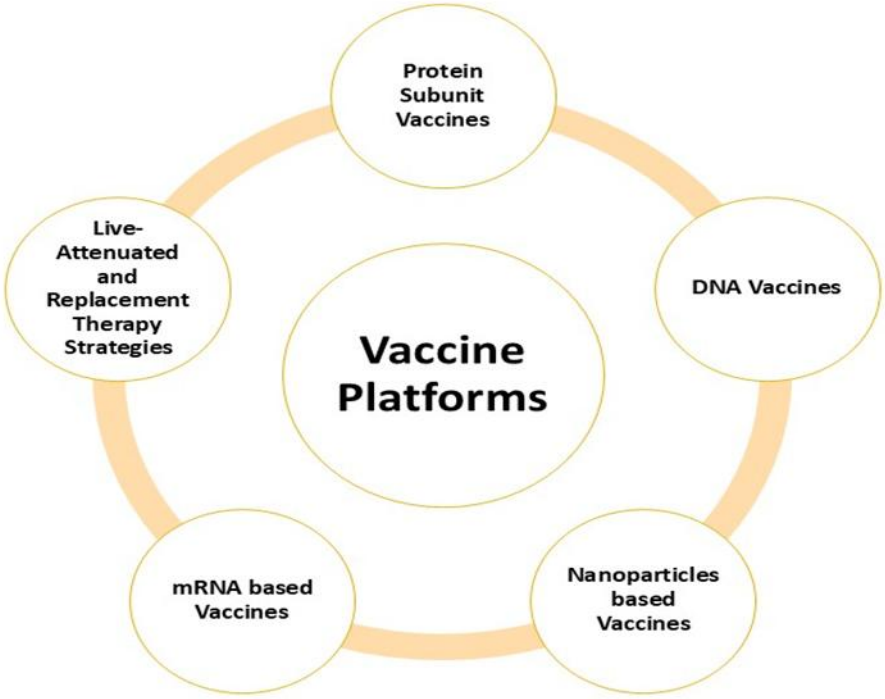

Figure 2: Vaccine Platforms for Dental Caries Vaccines

Protein subunit vaccines

Protein subunit vaccines are among the extensively studied vaccine formats for dental caries prevention. These vaccine formulations generally utilize purified or recombinant proteins (e.g., PAc, GTFs, or GBPs) as the immunogen.[26] The primary advantage of using subunit vaccines is the safety afforded by their use and their specificity. Subunit vaccines do not use whole bacterial cells minimizing the risk of infection. They are designed to target the harmful factors produced by *S. mutans.* However, the immunogenicity of protein subunit vaccines is often low, particularly when given by the mucosal route, and therefore it is necessary to use strong adjuvants or delivery systems to help enhance immune responses.[25]

DNA Vaccines

DNA vaccines represent a novel approach that involves the direct injection of plasmids encoding antigens of interest. One of the most studied DNA vaccines in this field is pGJA-P/VAX, which encodes the PAc antigen. When administered, these plasmids are taken up by host cells, which then express the antigen and present it to the immune system. DNA vaccines are stable, easy to produce, and capable of inducing both humoral and cell-mediated responses. Preclinical studies have demonstrated protective effects in animal models, and limited early-phase human trials have confirmed safety and immunogenicity. However, further optimization is needed for broader application in mucosal immunization.[16,27]

Nanoparticle-Based Vaccines

Nanotechnology has opened new avenues for vaccine delivery, particularly at mucosal surfaces. Nanoparticles made from materials such as chitosan, PLGA, or metal-organic frameworks (e.g., ZIF-8) can

encapsulate antigens and deliver them to antigen-presenting cells more efficiently. A recent study using ZIF-8 nanoparticles loaded with PAc antigen demonstrated significantly enhanced immune responses and caries protection in rats. These platforms can also serve as both carriers and adjuvants, offering controlled release and increased antigen stability. While still in experimental phases, nanoparticle-based vaccines show promise for future translation into human use.[28,29]

mRNA-Based Vaccines

Inspired by their success in COVID-19 immunization, mRNA vaccine platforms are being investigated for dental applications. These vaccines deliver synthetic mRNA encoding target antigens, which are then translated in host cells to stimulate immune responses. Their major advantages include rapid development, scalable production, and the absence of genomic integration risks. Although mRNA vaccines for dental caries remain in the conceptual and preclinical stages, their adaptability and potency make them a compelling option for future research.[30]

Live-Attenuated and Replacement Therapy Strategies

An alternative strategy involves using genetically modified strains of *S. mutans* with reduced virulence—such as gcrR-deficient mutants—as a form of biological control. These strains can colonize the oral cavity and outcompete wild-type bacteria without contributing to acid production or caries formation. This approach, known as replacement therapy, offers a non-immunological yet ecological method of disease prevention. While promising in animal models, it raises concerns about long-term safety, horizontal gene transfer, and regulatory hurdles.[22]

VI. Routes Of Administration

The effectiveness of a dental caries vaccine is closely tied to the antigen and platform used and to the route by which it is delivered. Vaccine delivery strategies aim to stimulate strong local immune responses, particularly the production of secretory IgA antibodies in saliva. Researchers have investigated multiple mucosal and systemic routes throughout the years, each presenting unique immunological outcomes and logistical considerations.

Oral Route

Oral immunization is a natural and non-invasive delivery route that targets the immune response in the gastrointestinal-associated lymphoid tissue (GALT) site, such as the Peyer's patches. Oral immunization is advantageous in terms of patient compliance and safety, but it is compromised by the poor stability of antigens in the harsh gastric environment. Also, oral tolerance may inhibit the local immune response, while oral vaccination may cause tolerance through immune suppression. Encapsulation of antigens in protective carriers (liposomes, nanoparticles, etc.) is one way to overcome degradation and, hopefully, enhance uptake and immunogenicity.[31]

Nasal Route

Intranasal route provides direct access to the nasal-associated lymphoid tissue (NALT), which has immunological linkage to salivary glands. The clinical studies with nasal vaccines have demonstrated some promising results with local and systemic immune responses including increased levels of sIgA in saliva.It is a minimally invasive, non-gastrointestinal stable route of administration. However, concerns regarding central nervous system exposure, the mucosal irritation that might be associated with repeated intranasal dosing, influencing vaccine uptake need to be addressed.[18,31]

Sublingual and Buccal Routes

Sublingual and buccal immunizations, though less explored, provide the advantage of targeting the oral mucosa directly, without the need for antigen digestion or nasal penetration. These sites have rich vascular and lymphoid supply, which may facilitate rapid immune activation. Preliminary studies indicate that sublingual delivery of antigen-adjuvant combinations can successfully induce sIgA and systemic IgG responses. These routes may also be ideal for pediatric delivery due to ease of use and low invasiveness.

Systemic Routes (Intramuscular/Subcutaneous)

Systemic administration is the most established method in conventional vaccination, typically producing strong IgG responses. While systemic routes have been used in early dental caries vaccine trials, they are generally less effective at inducing salivary IgA unless paired with mucosal boosters. Nevertheless, they may still play a role in prime-boost strategies or multicomponent vaccines targeting both mucosal and systemic arms of immunity.

Gingivo-Salivary Route

A novel and highly targeted method, the gingivo-salivary route involves direct application of vaccines to the gingival sulcus, stimulating local immune tissues in the oral cavity. Though still experimental, this technique may offer precise immunological targeting while minimizing systemic exposure.[31]

VII. Adjuncts And Alternative Strategies

In addition to vaccines targeting *Streptococcus mutans*, several adjunct strategies have emerged to enhance protection against dental caries. Probiotics like *Lactobacillus* and *Streptococcus salivarius* may reduce cariogenic bacteria and support a healthier oral microbiome.[32] Natural products, including extracts from green tea, neem, and propolis, exhibit anti-*S. mutans* and anti-biofilm activity, and may serve as adjuvants.[33] Cannabinoids and oxygen-releasing gels are also being studied for their antimicrobial properties.[34] Lastly, behavioral measures—like sugar reduction, fluoride use, and oral hygiene—remain essential and should complement immunization strategies.[2]

Together, these approaches can support comprehensive caries prevention, particularly where vaccine access or coverage is limited.

VIII. Clinical Trials And Current Status

Although preclinical studies have shown that vaccines targeting *S. mutans* antigens like PAc, GTFs, and GBPs can reduce caries in animal models, progress in human trials has been limited.[35] Early Phase I and II trials using mucosal delivery (oral or intranasal) have demonstrated safety and the ability to stimulate salivary IgA and systemic IgG.[36] DNA-based vaccines such as pGJA-P/VAX and liposome-adjuvanted formulations have shown promise, yet none have advanced to Phase III or received regulatory approval.[27] Globally, active clinical trials are scarce, with more attention given to non-vaccine caries prevention methods like fluoride and probiotics.[16]

IX. Challenges In Vaccine Development

Developing a dental caries vaccine faces several hurdles. Mucosal immunity is difficult to stimulate effectively, and achieving sustained salivary IgA without triggering tolerance or inflammation remains challenging.[37] Vaccine antigens, such as PAc and GTFs, often elicit modest immune responses.[35] There is also antigenic variability among *S. mutans* strains. First, delivery routes that may include oral and nasal routes also require formulations to preserve the antigen and elicit the intended immune response. Safety and regulatory issues surrounding adjuvants further complicate vaccine development.[16,36] There are also ethical considerations for pediatric studies, the high cost of production, and the lack of market incentives for a vaccine for a non-life threatening infection like caries. Involvement from public health organizations will also be required to further vaccine development. Any advancement will best be realized with innovative thinking, collaborative enterprises, and strategically directed resources that result in a clinically viable vaccine for dental caries.[28]

X. Future Directions And Future Recommendations

Future progress in the development of a vaccine against dental caries will depend on utilising modern technologies and approaches and utilizing a multidisciplinary approach. Next generation nanoparticle carriers, mRNA platforms, and future mucosal adjuvants create opportunities for antigen delivery and eliciting immune responses. Multivalent formulations containing relevant antigens such as PAc, GTFs, and GBPs offer the opportunity for greater protection and addressing strain variability.

Clinical translation will benefit from ethical pediatric studies, clarity around regulatory pathways to approval, and heightened involvement of public health initiatives advocating for oral and dental health. The nature of dental caries and individual patient needs do not always align with public health goals. This gap supports the need for combination strategies that integrate vaccines with adjunct approaches such as probiotics, dietary management, and fluoride use. Together, these can form a more comprehensive caries prevention model. Advancing caries vaccines from theory to practice will require sustained research investment, collaboration between academic and industry sectors, and stronger prioritization of global oral health initiatives.

XI. Conclusion

The scientific foundation, recent developments, and challenges associated with the development of a vaccine against dental caries are highlighted in this review. The objective was to give an extensive understanding of the current state of the field and what is required to progress by looking at important antigens, delivery systems, clinical trial data, and supplementary approaches. Current developments in immunology and biotechnology present encouraging paths even in the absence of a vaccine that is ready for the market. Finding a safe, practical, and affordable solution for long-term caries control requires ongoing interdisciplinary research and integration with current preventive measures.

CONFLICT OF INTEREST: NIL

SOURCE OF FUNDING: NIL

ETHICAL STATEMENT: Not Applicable

References

[1] Li Z, Yu C, Chen H. Global, Regional, And National Caries Of Permanent Teeth Incidence, Prevalence, And Disability-Adjusted Life Years, 1990-2021: Analysis For The Global Burden Of Disease Study. BMC Oral Health. 2025 May 13;25(1):715.
[2] Han SY, Chang CL, Wang YL, Wang CS, Lee WJ, Vo TT, Chen YL, Cheng CY, Lee IT. A Narrative Review On Advancing Pediatric Oral Health: Comprehensive Strategies For The Prevention And Management Of Dental Challenges In Children. Children. 2025 Feb 26;12(3):286.
[3] Wu J, Chen J, Lv C, Zhou L. Global, Regional, And National Levels And Trends In Burden Of Dental Caries And Periodontal Disease From 1990 To 2035: Result From The Global Burden Of Disease Study 2021. BMC Oral Health. 2025 May 29;25(1):844.
[4] Spatafora G, Li Y, He X, Cowan A, Tanner ACR. The Evolving Microbiome Of Dental Caries. Microorganisms. 2024 Jan 7;12(1):121.
[5] Laroche E. Management Practices That Promote Preventive Measures Compliance: A Comparative Analysis Between Hospital Healthcare Workers And Teachers. Safety Science. 2024 Sep 1;177:106591.
[6] Scharnow AM, Solinski AE, Wuest WM. Targeting S. Mutans Biofilms: A Perspective On Preventing Dental Caries. Medchemcomm. 2019 Mar 19;10(7):1057-1067.
[7] Chen X, Daliri EB, Kim N, Kim JR, Yoo D, Oh DH. Microbial Etiology And Prevention Of Dental Caries: Exploiting Natural Products To Inhibit Cariogenic Biofilms. Pathogens. 2020 Jul 14;9(7):569.
[8] Bowen WH, Koo H. Biology Of Streptococcus Mutans-Derived Glucosyltransferases: Role In Extracellular Matrix Formation Of Cariogenic Biofilms. Caries Res. 2011;45(1):69-86.
[9] Michalek SM, Katz J, Childers NK. A Vaccine Against Dental Caries: An Overview. Biodrugs. 2001;15(8):501-8.
[10] Gao Z, Chen X, Wang C, Song J, Xu J, Liu X, Qian Y, Suo H. New Strategies And Mechanisms For Targeting Streptococcus Mutans Biofilm Formation To Prevent Dental Caries: A Review. Microbiol Res. 2023 Oct 14;278:127526.
[11] Yu YB, Liu Y, Li S, Yang XY, Guo Z. The Ph-Responsive Zeolitic Imidazolate Framework Nanoparticle As A Promising Immune-Enhancing Adjuvant For Anti-Caries Vaccine. J Dent. 2023 Mar;130:104413.
[12] Jia R, Guo JH, Fan MW, Bian Z, Chen Z, Peng B, Fan B. Mucosal Immunization Against Dental Caries With Plasmid DNA Encoding Pac Gene Of Streptococcus Mutans In Rats. Vaccine. 2004 Jun 30;22(20):2511-6.
[13] Liu B, Li M, Li X, Yang J, Yan H. An Optimized Caries Model Of Streptococcus Mutans In Rats And Its Application For Evaluating Prophylactic Vaccines. Human Vaccines & Immunotherapeutics. 2024 Dec 31;20(1):2345943.
[14] Ay C, Karayılmaz H, Cengiz A. Early Oral Colonization Of Streptococcus Mutans And Lactobacilli Species In Infants: Investigating The Relationship With Maternal And Environmental Factors, From Birth Through The Sixth Month. Pak J Med Sci. 2024 Oct;40(9):2028-2035.
[15] Amanna IJ, Slifka MK. Contributions Of Humoral And Cellular Immunity To Vaccine-Induced Protection In Humans. Virology. 2011 Mar 15;411(2):206-15.
[16] Patel M. Dental Caries Vaccine: Are We There Yet? Lett Appl Microbiol. 2020 Jan;70(1):2-12.
[17] Yarmola E, Ishkov IP, Di Cologna NM, Menashe M, Whitener RL, Long JR, Abranches J, Hagen SJ, Brady LJ. Amyloid Aggregates Are Localized To The Nonadherent Detached Fraction Of Aging Streptococcus Mutans Biofilms. Microbiol Spectr. 2022 Aug 31;10(4):E0166122
[18] Su LK, Yu F, Li ZF, Zeng C, Xu QA, Fan MW. Intranasal Co-Delivery Of IL-6 Gene Enhances The Immunogenicity Of Anti-Caries DNA Vaccine. Acta Pharmacol Sin. 2014 May;35(5):592-8.
[19] Zhang Q, Ma Q, Wang Y, Wu H, Zou J. Molecular Mechanisms Of Inhibiting Glucosyltransferases For Biofilm Formation In Streptococcus Mutans. Int J Oral Sci. 2021 Sep 30;13(1):30.
[20] Smith DJ, Taubman MA. Experimental Immunization Of Rats With A Streptococcus Mutans 59-Kilodalton Glucan-Binding Protein Protects Against Dental Caries. Infect Immun. 1996 Aug;64(8):3069-73
[21] Banas JA, Vickerman MM. Glucan-Binding Proteins Of The Oral Streptococci. Crit Rev Oral Biol Med. 2003;14(2):89-99.
[22] Gupta S, Marwah N. 'Use A Thorn To Draw Thorn' Replacement Therapy For Prevention Of Dental Caries. Int J Clin Pediatr Dent. 2010 Sep-Dec;3(3):125-37
[23] Chen H, Yang Y, Weir MD, Dai Q, Lei L, Homayounfar N, Oates TW, Yang K, Zhang K, Hu T, Xu HHK. Regulating Oral Biofilm From Cariogenic State To Non-Cariogenic State Via Novel Combination Of Bioactive Therapeutic Composite And Gene-Knockout. Microorganisms. 2020 Sep 13;8(9):1410.
[24] Sun Y, Yang Y, Zhou D, Cao Y, Yu J, Zhao B, Zhong M, Li Y, Yang J, Yan H. Flagellin-Rpac Vaccine Inhibits Biofilm Formation But Not Proliferation Of S. Mutans. Hum Vaccin Immunother. 2016 Nov;12(11):2847-2854.
[25] Contreras S, Mayta-Tovalino F, Munive-Degregori A, Mendoza R, Barja-Ore J, Mauricio-Vilchez C. Anticaries Vaccine As A Promising Alternative For Protection Against Dental Caries: A Literature Review. Journal Of International Oral Health. 2023 Jan 1;15(1):34-42.
[26] Smith DJ, King WF, Rivero J, Taubman MA. Immunological And Protective Effects Of Diepitopic Subunit Dental Caries Vaccines. Infect Immun. 2005 May;73(5):2797-804.
[27] Liu C, Fan M, Bian Z, Chen Z, Li Y. Effects Of Targeted Fusion Anti-Caries DNA Vaccine Pgja-P/VAX In Rats With Caries. Vaccine. 2008 Dec 2;26(51):6685-9.
[28] Yu YB, Liu Y, Liang H, Dong X, Yang XY, Li S, Guo Z. A Nanoparticle-Based Anticaries Vaccine Enhances The Persistent Immune Response To Inhibit Streptococcus Mutans And Prevent Caries. Microbiol Spectr. 2023 Mar 28;11(2):E0432822.
[29] Qu S, Ma X, Yu S, Wang R. Chitosan As A Biomaterial For The Prevention And Treatment Of Dental Caries: Antibacterial Effect, Biomimetic Mineralization, And Drug Delivery. Front Bioeng Biotechnol. 2023 Sep 29;11:1234758.
[30] Koren L, Koren A, Likić R, Katanec T. Revolutionizing Dentistry: Preclinical Insights And Future Applications Of Mrna Vaccines In Dentistry-A Narrative Review. Dent J (Basel). 2025 Feb 13;13(2):79.
[31] Shivakumar KM, Vidya SK, Chandu GN. Dental Caries Vaccine. Indian J Dent Res. 2009 Jan-Mar;20(1):99-106.
[32] Luo SC, Wei SM, Luo XT, Yang QQ, Wong KH, Cheung PCK, Zhang BB. How Probiotics, Prebiotics, Synbiotics, And Postbiotics Prevent Dental Caries: An Oral Microbiota Perspective. NPJ Biofilms Microbiomes. 2024 Feb 24;10(1):14

[33] Kashi M, Varseh M, Hariri Y, Chegini Z, Shariati A. Natural Compounds: New Therapeutic Approach For Inhibition Of Streptococcus Mutans And Dental Caries. Front Pharmacol. 2025 Apr 1;16:1548117.
[34] Aqawi M, Steinberg D, Feuerstein O, Friedman M, Gingichashvili S. Cannabigerol Effect On Streptococcus Mutans Biofilms-A Computational Approach To Confocal Image Analysis. Front Microbiol. 2022 Apr 29;13:880993.
[35] Smith DJ. Dental Caries Vaccines: Prospects And Concerns. Crit Rev Oral Biol Med. 2002;13(4):335-49.
[36] Kt S, Kmk M, N B, Jimson S, R S. Dental Caries Vaccine - A Possible Option? J Clin Diagn Res. 2013 Jun;7(6):1250-3
[37] Taubman MA, Nash DA. The Scientific And Public-Health Imperative For A Vaccine Against Dental Caries. Nat Rev Immunol. 2006 Jul;6(7):555-63