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DENTAL CARIES VACCINES: A SHIFT FROM RESTORATIVE TO PREVENTIVE STRATEGY

Dentistry

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ABSTRACT

Dental caries is a chronic infectious disease affecting populations worldwide. Traditional approaches focus on mechanical and chemical prevention, yet the prevalence remains high, especially in children. Recent advancements in immunology and microbiology suggest that vaccination targeting Streptococcus mutans, the primary etiological agent in dental caries, could offer long-lasting immunity. This review evaluates key antigens, immunization strategies, delivery systems, and the clinical potential of both active and passive immunization in the context of oral health.

KEYWORDS

Dental Caries, Caries Vaccine, Passive Immunization, Active Immunization.

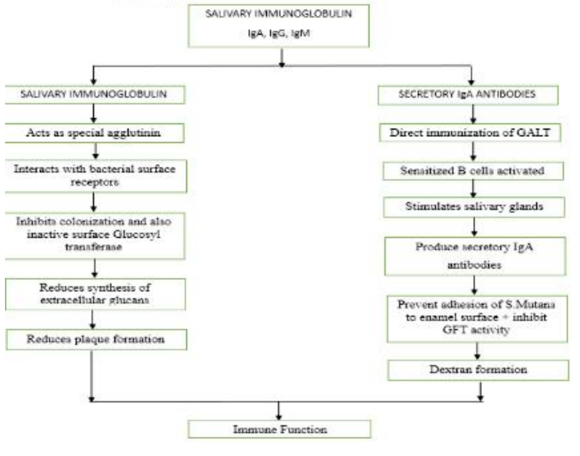
INTRODUCTION

Dental caries is a highly prevalent chronic infectious disease affecting all age groups. It results from the interaction of cariogenic bacteria, dietary sugars, host factors, and time, leading to demineralization of tooth structure. *Streptococcus mutans* is the primary pathogen, with *Lactobacillus acidophilus* and *Actinomyces viscosus* contributing in advanced stages.(1) Globally, caries affects up to 90% of individuals in developed countries, with rising prevalence in developing regions.(2) It impacts nutrition, speech, quality of life, and imposes significant economic costs. Traditional restorative treatments manage existing lesions but do not prevent recurrence. Given these challenges, vaccine development targeting *S. mutans* has emerged as a promising preventive approach.(3)This review outlines the rationale, key antigens, delivery routes, and immunological strategies involved in caries vaccine development.

HISTORY OF VACCINES

Research on a dental caries vaccine began in the 1920s, with *S. mutans* identified as the primary pathogen by the 1960s. (4) Bowen's studies showed immunized monkeys had fewer cavities. Mestecky and others demonstrated that oral immunization could stimulate salivary IgA (S-IgA), reducing bacterial adhesion.(5)Guggenheim later identified glucosyltransferases (GTFs) as key targets for vaccine development. Despite technical challenges, animal studies showed reduced caries, and genome sequencing of *S. mutans* has advanced modern vaccine research.

MECHANISM OF ACTION(6,7)



APPROACHES OF CARIES VACCINE

A) Subunit Vaccines

Target specific S. mutans components like Ag I/II, GTFs, and GbpB to elicit focused immune responses without using whole bacteria. They can be engineered to avoid cross-reactivity with non-cariogenic flora.(8)

B) Synthetic Vaccines

Lab-made peptides from antigenic regions (e.g., alanine-rich Ag I/II) are used to induce mucosal and systemic immunity. Fusion proteins and adjuvants like CTB enhance protection, especially via intranasal or sublingual routes.(9)

C) Recombinant Vaccines / Attenuated Vectors

Utilize genetically modified vectors (e.g., Salmonella, E. coli) to express S. mutans antigens and stimulate strong, long-lasting mucosal and systemic responses. Chimeric fusions improve immunogenicity. (10)

D) Conjugate Vaccines

Combine peptide antigens with polysaccharides (e.g., glucans or tetanus toxoid) to enhance T-cell-dependent immunity. Effective in young children and capable of inducing both IgA and IgG responses.(11)

TABLE NO 1:- ADJUVANT AND DELIVERY SYSTEM

System/ Adjuvant	Description	Immune Effect	Advantages
Cholera Toxin (CT) / E. coli LT	Potent mucosal adjuvants; CTB or detoxified A1-subunit used to reduce toxicity	Enhances mucosal IgA response via nasal/oral routes	Strong immune boost; chimeric proteins improve safety
PLGA Microcapsules	Biodegradable particles for slow antigen release	Sustained mucosal (salivary) IgA production	Protects antigen; avoids inflammation; long-lasting effect
Nanoparticles	Chitosan-DNA complexes or anionic liposomes for DNA vaccine delivery	Induces mucosal and systemic immunity	Protects genetic material; targets nasal mucosa effectively
Liposomes	Phospholipid vesicles delivering antigens to mucosal tissues	5 times higher salivary IgA vs antigen alone	M-cell targeting; proven reduction in caries in animal models

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Chitosan	Cationic polysaccharide from chitin used for DNA protection and delivery	Enhances both humoral and cellular immunity	Adhesive, pH-responsive, biodegradable, boosts transfection
DNA Vaccines Plasmid DNA encoding S. mutans antigens injected directly Activates APCs and induces both T and B cell responses Easy to produce, stable, long-lasting expression, modifiable			

TABLE NO.2:- ANIMAL STUDIES ON CARIES VACCINE

Author / Year	Study Type	Subjects / Sample	Vaccine / Material Used	Route / Delivery System	Results
Martin et al., 2001	In vitro and mouse study	Cd4+ T cells and mice	CT A2/B + SBR chimeric vaccine	Intranasal / mucosal delivery	Boosted antibody response and B7-mediated T cell co-stimulation.
Xu et al., 2006	Animal Study	Mice, hamsters, rats, rabbits, monkeys	DNA vaccine: PGJA-P/VAX fusion antigen	Intramuscular / DNA-based delivery	Induced strong mucosal and systemic immunity; protection against *S. mutans.*
Jiang et al., 2013	Animal Study	Mice	Recombinant flagellin-PAc fusion protein (KFD2-rPAc)	ntranasal	Induced strong salivary IgA and reduced *S. mutans* colonization
Yu et al, 2019	Animal Study	Mice	Recombinant *Salmonella* expressing Ag I/II and CTB	Oral	High salivary IgA, strong protection against *S. mutans*
Liu et al., 2020	Animal Study	Rats	ZIF-8@PAc nanoparticle vaccine	Intranasal / nano-metal organic framework	Prolonged mucosal immunity, reduced caries scores, safe delivery system.
Zhou et al., 2022	Animal study	Mice	Chitosan + PAc with Pam3CSK4 / MPLA adjuvants	Nasal	Induced strong mucosal IgA and systemic IgG responses with minimal toxicity.

HUMAN STUDIES ON CARIES VACCINES

Although most caries vaccine research has been conducted in animal models, several early-phase human studies have explored the safety and immunogenicity of candidate vaccines. One of the most notable trials was conducted by Childers et al. (1999), where a crude *Streptococcus mutans* glucosyltransferase (C-GTF) antigen was administered intranasally to healthy adults, both with and without liposomal encapsulation. This study observed a significant 5-fold increase in nasal IgA, with moderate increases in salivary and serum IgA/IgG, indicating successful mucosal and systemic immune stimulation.(7)

Other early investigations explored oral delivery of GTF antigens using enteric-coated capsules, often derived from *S. sobrinus*. These studies showed that salivary secretory IgA (sIgA) responses could be induced following ingestion, particularly when formulated with adjuvants like alum. Work by Smith and Taubman (1987–1990) showed that oral GTF immunization delayed the recolonization of mutans streptococci after dental prophylaxis.(8) Similarly, Childers et al. (1994) used liposome-encapsulated GTF antigens and reported parotid IgA2 responses in most subjects. However, some studies—like those by Gahnberg and Krasse—reported minimal or no significant immune response when heat-killed *S. sobrinus* was administered orally.(6)

Topical mucosal immunization, including application to the lip mucosa or tonsils, has also shown promise. These routes facilitated targeted antigen exposure to local immune tissues, resulting in enhanced sIgA production and delayed re-colonization by *S. mutans*.(5)

Overall, these human studies confirm that mucosal immunization against dental caries is feasible and can stimulate protective antibody responses. However, most studies have been small in scale, focused on immunological endpoints rather than clinical outcomes like caries reduction. Larger, long-term clinical trials are still needed to evaluate real-world vaccine efficacy and safety.(12)

CONCLUSION

The quest for a dental caries vaccine is progressing steadily, supported by advances in immunology, molecular biology, and material science. Both active and passive strategies show substantial promise.(11) The ideal vaccine will be safe, easy to administer, cost-effective, and induce long-term mucosal immunity. While clinical application in humans is still under development, particularly for pediatric use, the foundation laid by animal studies is strong. With continued investment in research, a caries vaccine could become a game-changer in global oral health.(13)

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