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Innovations in dental caries vaccination: Current research, challenges, and future prospects

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Abstract
Dental caries remains a widespread global health concern, affecting individuals across all age groups. Despite advancements in preventive dentistry, such as fluoride treatments and improved oral hygiene, the disease continues to be a leading cause of tooth decay and loss. The development of a caries vaccine presents a promising approach to combat this issue by targeting key cariogenic bacteria, primarily Streptococcus mutans. This article reviews the historical background, molecular targets, vaccine types, administration routes, recent advancements, and associated risks. Drawing insights from recent research findings, we explore the feasibility of a dental caries vaccine as a viable public health intervention, highlighting its potential for long-term prevention and improved global oral health outcomes.

Keywords: Dental carries vaccine, streptococcus mutans, passive immunization, glucosyltransferase (GTF), IGY immunoglobulin

Introduction

The Burden of Dental Caries

Dental caries is a chronic, multifactorial disease resulting from an imbalance between demineralization and remineralization of the tooth enamel. It is primarily caused by acidogenic bacteria, notably Streptococcus mutans, which ferment dietary carbohydrates into acids, leading to enamel breakdown [21].

The World Health Organization (WHO) has classified dental caries as a major public health problem, with a global prevalence of over 60% among school-aged children and a significant burden on adult populations. The Global Burden of Disease Study (2017) identified dental caries as one of the most common diseases worldwide, affecting nearly 2.4 billion individuals [22].

The Need for a Dental Caries Vaccine

Despite the availability of fluoride treatments, pit and fissure sealants, and improved oral hygiene practices, the prevalence of caries remains high. Several limitations exist:

- Fluoride does not prevent bacterial colonization but only slows enamel demineralization.
- Mechanical plaque removal is not fully effective, especially in high-risk populations.
- Oral health disparities in developing regions make preventive care less accessible.

A dental caries vaccine could offer a long-term, cost-effective solution by inducing immune protection against cariogenic bacteria, reducing their ability to colonize the oral cavity.

The Microbial Basis of Dental Caries

Key Cariogenic Bacteria

Dental caries is primarily caused by a group of acidogenic bacteria:

- Streptococcus mutans – the principal pathogen responsible for initiating caries.
- Lactobacillus species – contribute to lesion progression.
- Actinomyces viscosus – associated with root caries.

These bacteria produce lactic acid through the fermentation of carbohydrates, lowering the oral pH and triggering demineralization of enamel [25].

Mechanism of Caries Formation

1. Bacterial Adhesion – S. mutans binds to the tooth surface via adhesins (AgI/II protein) [11].
2. Biofilm Formation – S. mutans produces extracellular polysaccharides (EPS) through glucosyltransferase (GTFs), enhancing bacterial accumulation.
3. Acid Production – Fermentation of sugars results in lactic acid, which dissolves enamel minerals.4. Cavity Progression – Continuous demineralization leads to cavity formation and tooth decay.

Given the central role of S. mutans in caries development, targeting its virulence factors is a promising approach for vaccine development [3].

Historical Perspective on Caries Vaccination

The idea of a dental caries vaccine dates back to the 1960s, when researchers identified S. mutans as a primary etiologic agent. Key milestones include:

- 1969 – Bowen successfully vaccinated monkeys using intravenous S. mutans, reducing caries formation.
- 1970s–1980s – Identification of secretory IgA (sIgA) as a key immune component in oral defenses.
- 1990s–2000s – Development of subunit vaccines targeting glucosyltransferases (GTFs), adhesins, and glucan-binding proteins (GBPs).

Recent Advances: Use of recombinant DNA, synthetic peptides, and nanoparticle-based delivery systems for enhanced immune response.

Molecular Targets for Caries Vaccination

Recent research has focused on three primary molecular targets for vaccine development:

1. Glucosyltransferase (GTFs)
Key enzyme responsible for glucan synthesis, facilitating biofilm formation.
Vaccines targeting GTFs aim to disrupt biofilm stability, reducing bacterial adherence [16].

2. Glucan-Binding Proteins (GBPs)
Play a role in plaque accumulation by binding glucans.
Vaccination against GBPs prevents bacterial clustering, reducing cariogenic potential [17].

3. Adhesins (AgI/II, PAc Protein)
Mediate bacterial adhesion to tooth enamel.
Blocking these proteins inhibits bacterial colonization [15, 18]

Types of Dental Caries Vaccines
Active Immunization
Active vaccines stimulate host immunity to produce protective antibodies against S. mutans. Prominent candidates include:
Subunit Vaccines – Targeting GTF, GBP, and PAc proteins.
Conjugate Vaccines – Linking bacterial antigens to carrier proteins for enhanced immune response.
Recombinant DNA Vaccines – Delivering genetic material to produce anti-caries antigens within the body.

Passive Immunization
Passive immunization involves the external administration of preformed antibodies, such as:
Egg Yolk-Derived IgY Antibodies – Applied via lozenges, mouth rinses, or toothpaste to neutralize S. mutans [7, 9].
Transgenic Plant-Derived Antibodies – Produced in genetically modified plants to provide oral protection.

Routes of Vaccine Administration
The success of a dental caries vaccine depends on its delivery method. Current research explores:
Oral Vaccination – Stimulating gut-associated lymphoid tissue (GALT) to induce mucosal immunity.
Intranasal Vaccination – Activating nasal-associated lymphoid tissue (NALT) for a localized immune response.
Tonsillar Application – Generating salivary IgA responses via topical antigen exposure.
Among these, intranasal and oral routes have shown the most promising results in preclinical studies.

Recent Advances in Caries Vaccine Research
Nanoparticle-Based Vaccines
Nanoparticles enhance antigen stability and immune response.
ZIF-8 nanoparticles loaded with PAc protein zeolitic imidazolate framework-8 nanoparticle (ZIF-8 NP)-based adjuvant with good biocompatibility, pH responsiveness, and high loading performance for PAc that was used as an anticaries vaccine [10].

Synthetic Peptide Vaccines
Peptide-based vaccines elicit specific immunity against key S. mutans antigens.
Intranasal immunization with PAc peptides has successfully reduced bacterial colonization.

DNA and Recombinant Vaccines
Fusion DNA vaccines combining PAc and glucosyltransferase domains have demonstrated long-term protection.
Recombinant Salmonella-based oral vaccines have elicited strong mucosal immunity.

Risks and Challenges
Safety Concerns
- Potential for autoimmunity due to cross-reactivity with human tissues. Long-term immune memory remains a challenge.
- Regulatory and Ethical Considerations
- Clinical trials are needed to assess human safety and efficacy.
- Public perception and acceptance require targeted education efforts.

Conclusion
The development of a dental caries vaccine represents a transformative approach to preventing tooth decay. By targeting S. mutans virulence factors, vaccines have the potential to provide long-term immunity, especially in high-risk populations. While significant progress has been made, further clinical trials and regulatory approvals are needed before widespread implementation. Future research should focus on optimizing antigen delivery, ensuring long-term efficacy, and addressing safety concerns.
A successful dental caries vaccine could revolutionize preventive dentistry, reducing global caries burden and improving oral health outcomes worldwide.

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Conflicts of interest
There are no conflicts of interest.

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