

MUCOSAL VACCINES AND NEEDLE-FREE IMMUNISATION

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ABSTRACT

Conventional injectable vaccines have transformed infectious-disease prevention, but they do not always generate strong immune responses at the mucosal surfaces through which many pathogens enter the body. Mucosal vaccination aims to place vaccine antigens at or near these portals of entry and can stimulate local secretory IgA, tissue-resident cellular responses and systemic immunity. At the same time, needle-free and non-invasive delivery approaches can reduce pain and needle-related waste, simplify administration and potentially improve acceptability and access. Recent research has expanded the field from traditional oral and intranasal formulations toward nanoparticles, lipid-based carriers, chitosan systems, virus-like particles, nucleic-acid platforms, thermostable formulations, dissolving films and other advanced delivery technologies.^[1-5] This review examines the immunological basis of mucosal vaccination, major administration routes, formulation and delivery strategies, needle-free technologies, adjuvants, barriers to translation and future opportunities. Particular attention is given to the pharmaceutical challenges of protecting antigens from degradation, overcoming mucus and epithelial barriers, achieving adequate residence time and inducing effective immunity without excessive inflammation. The review also discusses the importance of thermostability, scalable manufacturing, safety, dose consistency, regulatory evaluation and validated correlates of mucosal protection. Mucosal vaccination should not be viewed simply as a replacement for injections; rather, it represents a complementary platform capable of tailoring immunity to the site of pathogen entry. The next generation of vaccine delivery is likely to combine immunology, formulation science, biomaterials, nanotechnology and device engineering to create safer, more accessible and potentially more effective vaccination systems.

KEYWORDS: mucosal vaccines; needle-free immunisation; intranasal vaccines; oral vaccines; secretory IgA; vaccine delivery; nanocarriers; adjuvants; dissolving films; thermostable vaccines.

1. INTRODUCTION

Vaccination remains one of the most effective public-health interventions, but the conventional intramuscular or subcutaneous route is not optimal for every pathogen or every population. Many infectious agents initially interact with mucosal surfaces of the respiratory,

gastrointestinal or genitourinary tract. Mucosal vaccination is therefore attractive because antigen exposure at these sites can generate local immune responses in addition to systemic immunity.^[1,2]

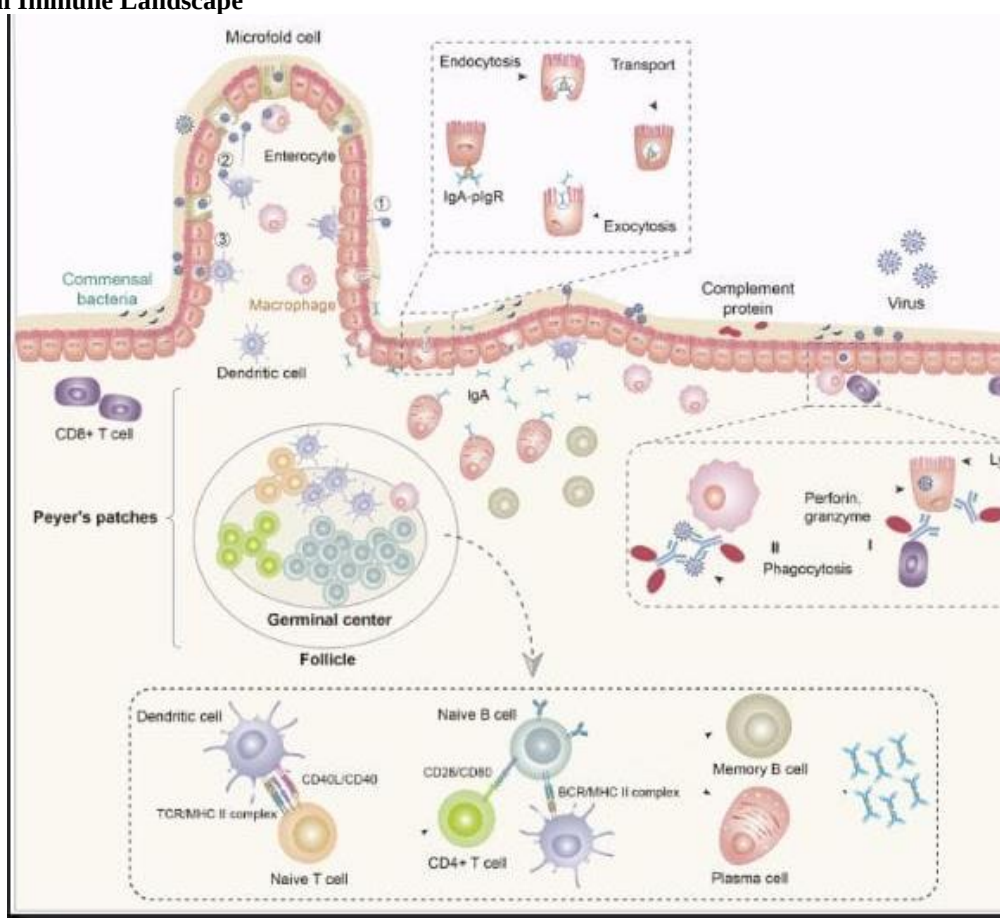
Needle-free delivery adds a second dimension: it can reduce pain and needle fear, avoid sharps waste and needle-stick injuries, and potentially facilitate administration outside conventional injection settings. However, needle-free does not automatically mean non-invasive. Jet injectors, for example, deliver formulations through the skin without a conventional needle, whereas oral, intranasal and buccal routes are genuinely mucosal approaches.^[3]

The field is evolving rapidly. A 2026 review in *npj Vaccines* highlighted chitosan nanoparticles as promising carriers for mucosal and needle-free vaccination, while a recent review of mucosal vaccine development described intranasal, oral and sublingual routes alongside nanoparticles, lipid nanoparticles, virus-like particles and engineered bacterial platforms.^[4,5] These developments justify a modern review centred on the convergence of mucosal immunology and pharmaceutical delivery science.

2. Why Move Beyond the Needle?

Conventional injection challenge	Potential needle-free advantage	Remaining question
Pain and needle fear	Potentially painless administration	Will acceptability translate into higher uptake?
Sharps waste	Reduced or eliminated sharps	What are device/formulation disposal requirements?
Needle-stick injury	Lower risk with non-needle routes	What safety risks replace them?
Need for trained personnel	Some routes may simplify administration	Can dose accuracy be maintained?
Limited mucosal immunity	Mucosal routes can target entry surfaces	Can protection be sufficiently durable?

3. The Mucosal Immune Landscape



Mucosal surfaces are protected by mucus, epithelial barriers, antimicrobial molecules, innate immune cells and organised lymphoid structures. Vaccine antigens must reach appropriate antigen-presenting cells while avoiding rapid clearance or degradation. Mucosa-associated lymphoid tissues, including nasal-associated

and gut-associated lymphoid tissues, provide sites where antigen sampling can initiate adaptive responses.^[1,2]

A major desired outcome is secretory immunoglobulin A (sIgA), which can bind pathogens and toxins at mucosal surfaces. Mucosal vaccination may also support local T-

cell responses and systemic antibody responses. However, the magnitude and durability of mucosal immunity depend on route, antigen, formulation, adjuvant, dose and host factors.

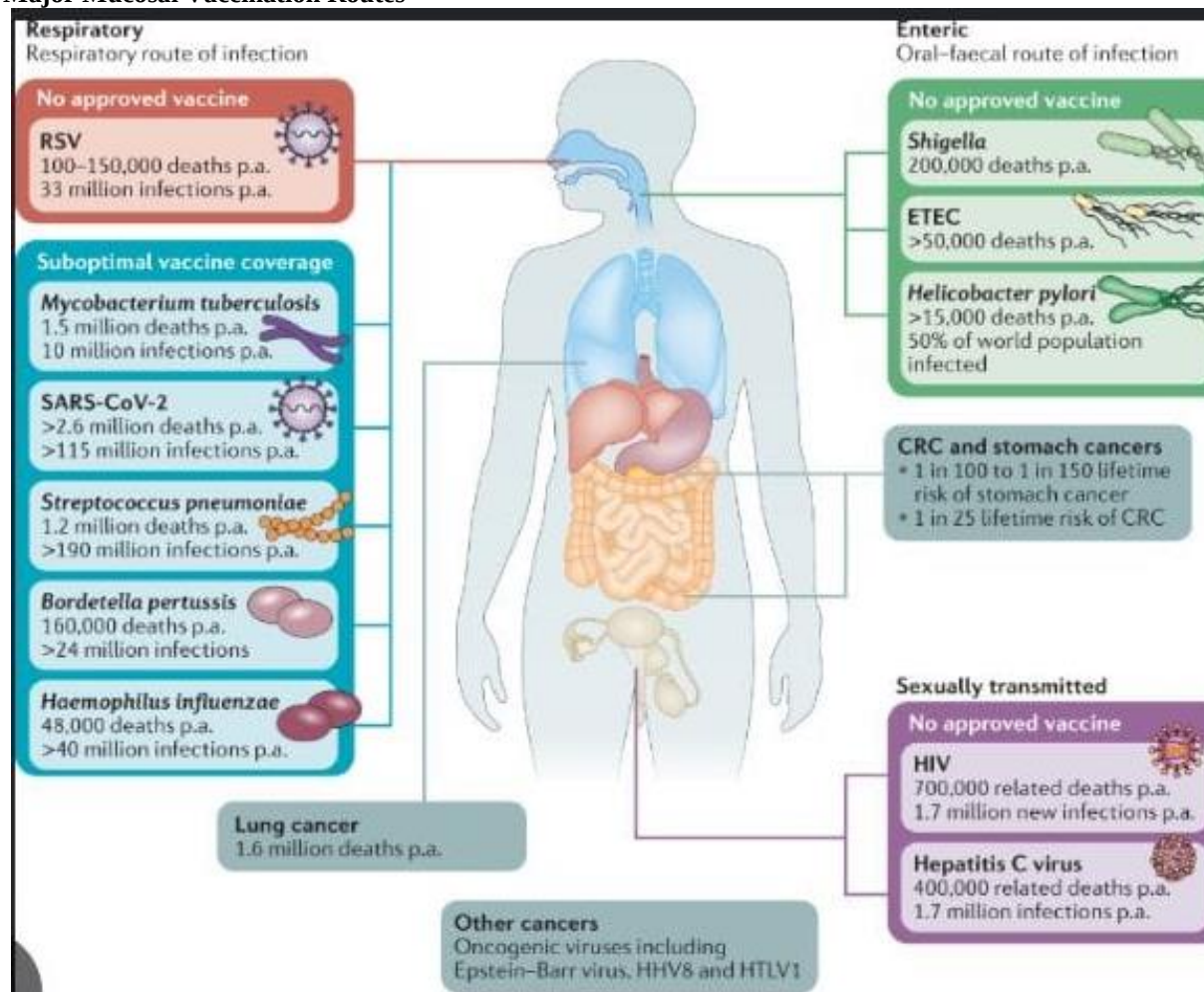
4. The Central Pharmaceutical Problem: Getting the Antigen to the Immune System

Mucosal delivery is difficult because the same barriers that protect the body from pathogens also limit vaccine delivery. Mucus can trap and clear particles; enzymes

and low pH can degrade proteins and nucleic acids; epithelial tight junctions restrict transport; and some mucosal tissues have tolerogenic characteristics.^[1,6]

An effective formulation therefore needs a coordinated strategy: protect the antigen, increase residence time, facilitate uptake, activate suitable innate pathways and release antigen in a manner that produces protective rather than excessive inflammation.

5. Major Mucosal Vaccination Routes



5.1 Intranasal Vaccination

The nasal route provides direct access to respiratory mucosa and nasal-associated lymphoid tissues. Intranasal formulations may be delivered as drops, sprays or other specialised devices. The route is particularly attractive for respiratory pathogens because it can generate local immunity near the initial site of exposure. Important formulation challenges include rapid mucociliary clearance, limited dosing volume, variability in nasal anatomy and the need to avoid unwanted distribution to sensitive tissues.

5.2 Oral Vaccination

The gastrointestinal tract offers a large immunological surface and contains organised lymphoid structures such

as Peyer's patches. However, oral vaccines must survive gastric acidity, digestive enzymes, bile and intestinal transit. Encapsulation, enteric protection, mucoadhesive systems and M-cell-targeting strategies have therefore been investigated.^[1,6]

5.3 Buccal and Sublingual Vaccination

The buccal and sublingual mucosae can provide relatively accessible surfaces for antigen delivery. Films, tablets, gels, nanoparticles and other systems have been investigated. The route may avoid some gastrointestinal degradation and can be patient-friendly, although saliva, swallowing and limited antigen residence time remain challenges.^[7]

5.4 Pulmonary and Aerosol Vaccination

The lungs provide a large surface area and specialised immune environment. Aerosolised vaccine delivery is conceptually attractive for respiratory infections, but particle size, deposition pattern, device performance, formulation stability and pulmonary safety require careful control.

6. Advanced Vaccine Delivery Platforms

6.1 Nanoparticle-Based Systems

Nanoparticles can protect antigens, modify release, increase mucosal residence and facilitate uptake by antigen-presenting cells. Materials under investigation include polymeric nanoparticles, lipid-based particles and other engineered nanocarriers. Their pharmaceutical advantages must be balanced against manufacturing complexity, stability and safety considerations.

6.2 Chitosan-Based Delivery

Chitosan is particularly interesting because of its mucoadhesive properties and potential to enhance mucosal antigen delivery. A 2026 npj Vaccines review highlighted chitosan nanoparticles as an emerging platform for improving antigen stability, mucosal delivery and immune activation.^[4]

6.3 Lipid Nanoparticles and Nucleic-Acid Vaccines

Lipid nanoparticles have become important in nucleic-acid delivery and are being investigated for mucosal vaccine applications. Their ability to protect RNA and facilitate cellular uptake makes them attractive, but route-specific stability, local tolerability and controlled immune activation remain important development questions.

6.4 Virus-Like Particles

Virus-like particles can present repetitive antigen structures that efficiently engage the immune system while lacking the complete infectious viral genome. Their highly organised architecture makes them attractive for vaccine design, although manufacturing and antigen-display consistency require careful control.

6.5 Dissolving Films and Solid Oral Platforms

Dissolving films, tablets and other solid dosage forms may improve portability and reduce dependence on conventional injection infrastructure. They may also support easier administration in selected populations. The critical formulation challenge is preserving antigen activity during manufacture and storage.

7. Needle-Free Immunisation Technologies



Technology	Mechanism	Key opportunity
Intranasal spray	Deposits formulation on nasal mucosa	Respiratory-site immunity
Oral/buccal film	Dissolves and releases antigen	Convenient administration
Jet injector	High-velocity liquid penetrates skin	Needle-free parenteral delivery
Microneedle patch	Microscopic projections deliver antigen	Minimal-pain skin delivery
Dry-powder/aerosol system	Delivers particles to respiratory tract	Potential thermostability and portability
Mucoadhesive nanoparticle	Extends mucosal residence and protects antigen	Improved local exposure

8. Adjuvants: Turning Exposure into Protective Immunity

A mucosal vaccine often requires more than antigen delivery. Adjuvants can enhance innate immune activation, antigen uptake and adaptive responses. Candidate approaches include toll-like receptor agonists, cytokine-based strategies, detoxified microbial components and formulation-based immune stimulators. The key challenge is achieving sufficient immune activation without excessive inflammation or tissue damage.

Mucosal adjuvant development must therefore consider route-specific biology. An adjuvant that is effective by injection may not have the same performance or safety profile on a mucosal surface.

9. Thermostability and the Cold-Chain Challenge

A major opportunity for next-generation vaccine formulations is improved stability outside conventional refrigerated conditions. Lyophilisation, dry powders, stabilising excipients, polymeric matrices and other formulation approaches are being investigated. Thermostable vaccines could simplify transport and improve access in settings where uninterrupted refrigeration is difficult. However, stability must be demonstrated for the complete antigen-delivery-device combination rather than inferred from laboratory storage alone.

10. The Most Important Barriers to Translation

10.1 Biological variability

Mucosal anatomy, mucus composition, age, microbiota and prior immunity can influence vaccine performance.

10.2 Antigen degradation

Proteins and nucleic acids can be damaged by enzymes, acidity and other environmental factors.

10.3 Limited residence time

Rapid mucus clearance may reduce the amount of antigen reaching immune-inductive sites.

10.4 Dose reproducibility

Small-volume nasal or oral products must deliver a consistent dose despite patient and device variability.

10.5 Safety

Local irritation, excessive inflammation, unwanted tissue exposure and formulation-related toxicity must be carefully assessed.

10.6 Correlates of protection

Systemic antibody titres do not always fully describe protection at mucosal surfaces. Recent reviews identify the absence of validated mucosal correlates as an important translational barrier.^[5]

10.7 Manufacturing and regulation

Scale-up, sterility where required, device compatibility, stability, quality control and regulatory pathways must be addressed early.

11. Mucosal Vaccine Development Pipeline: A Proposed Pharmaceutical Workflow

TARGET → ANTIGEN SELECTION → MUCOSAL ROUTE → BARRIER ANALYSIS → CARRIER/FORMULATION DESIGN → ADJUVANT SELECTION → DEVICE DESIGN → STABILITY TESTING → IMMUNOGENICITY → LOCAL SAFETY → CLINICAL PROTECTION → SCALE-UP

This workflow emphasises that mucosal vaccine development is not simply a formulation exercise. It is an integrated programme linking immunology, pharmaceuticals, device engineering, analytical science, clinical medicine and regulatory science.

12. Comparative Perspective of Mucosal Routes

Route	Main advantage	Major barrier	Potential immunity	Pharmaceutical focus
Nasal	Targets respiratory mucosa	Mucociliary clearance	Local + systemic	Spray, mucoadhesion, particle size
Oral	Highly acceptable	Acid/enzymes	Mucosal + systemic	Protection, targeting, stability
Buccal/sublingual	Accessible, non-invasive	Saliva/swallowing	Local + systemic	Films, tablets, residence time
Pulmonary	Large surface area	Deposition and safety	Respiratory	Aerosol engineering
Cutaneous microneedle	Minimal pain	Skin penetration/device	Systemic + potential mucosal effects	Patch design, dose uniformity

13. The Role of Pharmacists and Pharmaceutical Scientists

Mucosal vaccines are a multidisciplinary pharmaceutical problem. Pharmacists and pharmaceutical scientists can contribute to preformulation, excipient selection, dosage-form design, stability testing, analytical method development, quality control, device-formulation compatibility, patient counselling and pharmacovigilance. Their role is especially important when a vaccine moves from laboratory proof-of-concept to a reproducible dosage form.

For B.Pharm education, this field provides an opportunity to integrate pharmaceuticals, pharmacology, immunology, pharmaceutical analysis and regulatory science into a single translational topic.

14. Future Directions: What Could the Next Generation Look Like?

- Thermostable mucosal vaccines designed for reduced cold-chain dependence.
- Personalised or population-adapted formulations based on age, prior immunity and mucosal biology.
- Nanocarriers that combine antigen protection, targeting and controlled release.

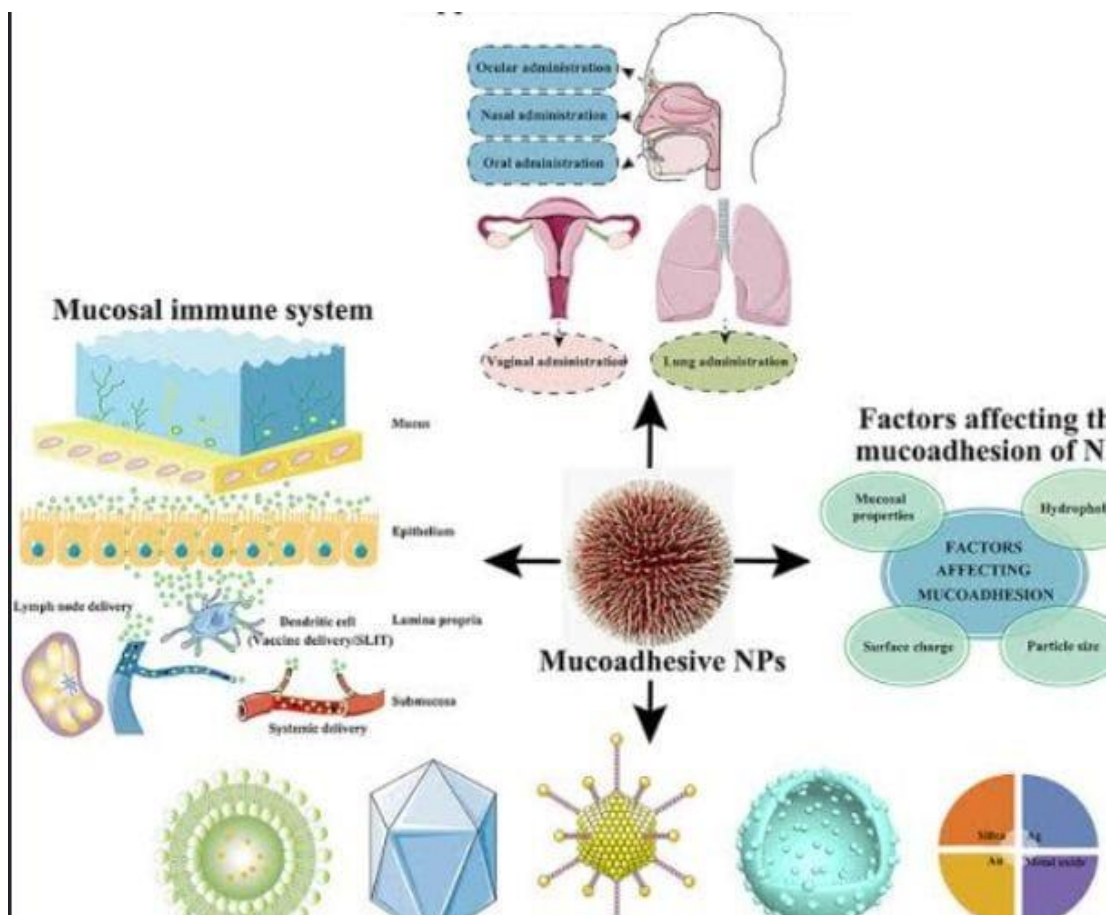
- AI-assisted optimisation of antigen–adjuvant–carrier combinations.
- Dry-powder and film-based dosage forms for simplified distribution.
- Combination vaccines capable of generating both systemic and mucosal immunity.
- Systems-biology approaches linking mucosal microbiota, innate signalling and vaccine response.
- Integrated device–formulation platforms designed for reliable self- or community administration where appropriate.

15. Role of Nanotechnology in Mucosal Vaccines

Nanotechnology is being investigated as a method for improving mucosal vaccine delivery. Nanoparticles and polymer-based systems can potentially protect antigens from degradation and improve their interaction with antigen-presenting cells.

Materials such as biodegradable polymers and chitosan have been studied as vaccine-delivery systems. These systems may help transport antigens across mucosal barriers and enhance immune recognition.

Other approaches include liposomes, polymeric particles, virus-like particles, and other antigen-delivery platforms.



16. Research Gaps Suitable for B.Pharm-Level Review and Future Projects

- Standardised methods for comparing mucosal residence time across formulations.
- Stability-indicating analytical methods for mucosal vaccine dosage forms.
- Comparative evaluation of mucoadhesive polymers for vaccine delivery.
- Formulation strategies for thermostable intranasal or oral vaccines.
- Relationship between particle characteristics and mucosal immune response.
- Patient acceptability of different needle-free vaccine dosage forms.
- Role of microbiota in variability of mucosal vaccine responses.
- Quality-by-design approaches for intranasal and oral vaccine manufacturing.

17. Limitations of the Review

This is a narrative review and does not constitute a systematic review or meta-analysis. The field is rapidly changing, and individual vaccine candidates, devices and regulatory pathways may progress after publication. Evidence from animal models cannot automatically be extrapolated to human clinical protection. Particular attention is therefore required when interpreting preclinical immunogenicity results.

18. CONCLUSION

Mucosal and needle-free vaccination represent an important direction in vaccine delivery because they address two distinct limitations of conventional injection: the need to stimulate immunity at pathogen-entry surfaces and the practical disadvantages associated with needles. Oral, intranasal, buccal, sublingual and pulmonary strategies can potentially produce local as well as systemic immune responses, while advanced carriers and devices may improve antigen protection, residence and delivery.

The next generation of vaccine delivery is unlikely to be defined by a single route or technology. Instead, progress will depend on rational integration of mucosal immunology, adjuvant science, nanotechnology, biomaterials, formulation engineering, device design and rigorous clinical evaluation. The central challenge is to translate promising laboratory systems into safe, stable, scalable and consistently protective products. For pharmaceutical sciences, mucosal vaccination therefore represents not only a new route of administration but a broad platform for innovation in vaccine design and delivery.

REFERENCES

1. Shakya AK, Chowdhury MYE, Tao W, Gill HS. Mucosal Vaccine Delivery: Current State and a Pediatric Perspective. *Journal of Controlled Release*, 2016; 240: 394–413. doi:10.1016/j.jconrel.2016.02.014.
2. Saroja CH, Lakshmi PK, Bhaskaran S. Recent trends in vaccine delivery systems: A review. *International Journal of Pharmaceutical Investigation*, 2011; 1(2): 64–74. doi:10.4103/2230-973X.82384.
3. Giudice EL, Campbell JD. Needle-free vaccine delivery. *Advanced Drug Delivery Reviews*, 2006; 58(1): 68–89. doi:10.1016/j.addr.2005.12.003.
4. Chen C, Zhang C, Zhu S, et al. Chitosan nanoparticles for mucosal and needle-free vaccination. *npj Vaccines*, 2026. doi:10.1038/s41541-026-01496-8.
5. Mucosal Vaccine Development: From Adjuvant Design to Next-Generation Delivery Strategies. PubMed-indexed review, 2026.
6. Non-Invasive Vaccines: Challenges in Formulation and Vaccine Adjuvants. *Vaccines*. 2023; 11. Review.
7. Buccal and Sublingual Vaccines: A Review on Oral Mucosal Immunization and Delivery Systems. *Pharmaceutics*, 2021.
8. Nanocarriers-Assisted Needle-Free Vaccine Delivery Through Oral and Intranasal Transmucosal Routes: A Novel Therapeutic Conduit. *Pharmaceutics*, 2022.
9. Donnelly RF. Vaccine delivery systems. *Human Vaccines & Immunotherapeutics*, 2017; 13(1): 17–18.
10. Lipid-Based Particles: Versatile Delivery Systems for Mucosal Vaccination against Infection. Review article, 2018.