IJMPR, 2026, 10(3), 15-18 ISSN: 2319-5878

INTERNATIONAL JOURNAL OF MODERN PHARMACEUTICAL RESEARCH

www.ijmpronline.com

Review Article

Impact Factor: 7.533

Coden USA: IJMPR3

A COMPREHENSIVE REVIEW ON NANOPARTICLE-BASED BUCCAL DRUG DELIVERY SYSTEMS

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Article Received on: 03/02/2026 **Article Revised on: 24/02/2026** **Article Published on: 01/03/2026**

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https://doi.org/10.5281/zenodo.18812470

How to cite this Article: Mrs. Swapnali Pankaj Mahajan*, Jatin Anil Sachdev, Sachin Sanjay Patil (2026). A Comprehensive Review On Nanoparticle-Based Buccal Drug Delivery Systems. International Journal of Modern Pharmaceutical Research, 10(3), 15–18.

ABSTRACT

The buccal route of drug delivery has gained increasing importance as an alternative to conventional oral administration due to its ability to bypass hepatic first-pass metabolism and enhance drug bioavailability. However, limitations such as low permeability and short residence time restrict its broader application. The integration of nanotechnology into buccal drug delivery systems has emerged as a promising strategy to overcome these challenges. Nanoparticles improve drug solubility, stability, mucoadhesion, and controlled release, thereby enhancing therapeutic efficacy. Various nanoparticulate carriers including polymeric nanoparticles, liposomes, solid lipid nanoparticles, nanostructured lipid carriers, and dendrimers have been extensively explored for buccal administration. This review provides a detailed overview of the anatomy and physiology of the buccal mucosa, mechanisms of drug absorption, types of nanoparticles used, formulation approaches, evaluation parameters, advantages, limitations, and future prospects of nanoparticle-based buccal drug delivery systems.

KEYWORDS: Buccal drug delivery, Nanoparticles, Mucoadhesive systems, Controlled drug release, Bioavailability, Nanotechnology.

1. INTRODUCTION

The effectiveness of any pharmaceutical therapy depends largely on the ability of the drug to reach its site of action at a therapeutically effective concentration. Conventional oral drug delivery systems often suffer from drawbacks such as enzymatic degradation in the gastrointestinal tract, variable absorption, and extensive first-pass hepatic metabolism. These limitations have prompted researchers to explore alternative routes of drug administration that can improve therapeutic outcomes and patient compliance. Among these routes, buccal drug delivery has emerged as a promising approach for both local and systemic drug delivery.[1]

The buccal mucosa offers several advantages, including ease of administration, rich vascularization, relatively low enzymatic activity, and the possibility of rapid drug absorption. Despite these benefits, buccal delivery is limited by factors such as low permeability of the epithelium and continuous salivary secretion, which can reduce drug residence time. To overcome these challenges, novel drug delivery systems have been developed, among which nanoparticle-based systems have gained considerable attention.[2,3] Nanotechnology involves the design and application of materials at the nanometer scale, offering unique physicochemical properties that enhance drug delivery. Nanoparticles can encapsulate drugs, protect them from degradation, enhance mucosal adhesion, and provide controlled release. The incorporation of nanoparticles into buccal drug delivery systems represents a significant advancement in pharmaceutical technology, enabling improved bioavailability and therapeutic efficiency of a wide range of drugs.[4,5]

2. Buccal Drug Delivery System

2.1 Anatomy and Physiology of Buccal Mucosa

The buccal mucosa lines the inner cheek and forms part of the oral cavity. It is composed of non- keratinized stratified squamous epithelium supported by a connective tissue layer known as the lamina propria. The thickness of the buccal epithelium ranges from 500 to 800 µm, making it more permeable than the skin but less permeable than the sublingual mucosa. The presence of a dense capillary network beneath the epithelium facilitates rapid systemic absorption of drugs. The buccal mucosa is continuously bathed in saliva, which maintains hydration and enzymatic activity. While saliva aids in drug dissolution, it can also lead to drug dilution and unintentional swallowing, thereby reducing drug bioavailability. Therefore, designing buccal formulations that can adhere to the mucosa and resist salivary washout is essential for effective drug delivery.[6,7]

Fig. 01: Nanoparticle Based Buccal Drug Delivery.[6]

2.2 Mechanism of Drug Absorption Through Buccal Mucosa

Drug absorption through the buccal mucosa occurs primarily via two pathways: the transcellular and paracellular routes. The transcellular pathway involves drug transport through epithelial cells and is favored by lipophilic drugs, whereas the paracellular pathway involves movement between cells and is mainly utilized by hydrophilic drugs. The tight junctions between epithelial cells limit paracellular transport, making permeability a major challenge in buccal drug delivery. Nanoparticles enhance buccal absorption by increasing the concentration gradient at the mucosal surface, facilitating close contact with epithelial cells, and in some cases opening tight junctions. Mucoadhesive nanoparticles further improve drug absorption by prolonging residence time at the site of administration.[8,9]

3. Nanoparticles in Buccal Drug Delivery

Nanoparticles are colloidal carriers with particle sizes typically ranging from 1 to 1000 nm. Their small size and large surface area allow efficient drug loading and interaction with biological membranes. In buccal drug delivery, nanoparticles serve as carriers that improve drug solubility, stability, and permeability while enabling controlled and sustained release. The physicochemical properties of nanoparticles such as size, surface charge, and hydrophobicity play a crucial role in determining their interaction with buccal mucosa. Positively charged nanoparticles are particularly effective due to electrostatic interaction with negatively charged mucin, resulting in enhanced mucoadhesion and prolonged residence time.[10,11]

4. Types of Nanoparticles Used in Buccal Drug Delivery

4.1 Polymeric Nanoparticles

Polymeric nanoparticles are widely used due to their biodegradability, biocompatibility, and versatility. Polymers such as chitosan, poly(lactic-co-glycolic acid) (PLGA), and alginate are commonly employed. Chitosan-based nanoparticles are particularly popular for buccal delivery because of their mucoadhesive and permeation-enhancing properties.[12,13]

4.2 Liposomes

Liposomes are spherical vesicles composed of phospholipid bilayers capable of encapsulating both hydrophilic and lipophilic drugs. Their structural similarity to biological membranes enhances drug penetration through the buccal mucosa. However, stability issues and limited drug loading capacity remain challenges associated with liposomal formulations.[14]

4.3 Solid Lipid Nanoparticles and Nanostructured Lipid Carriers

Solid lipid nanoparticles (SLNs) consist of a solid lipid matrix that provides controlled drug release and improved stability. Nanostructured lipid carriers (NLCs), developed as second- generation lipid nanoparticles, incorporate both solid and liquid lipids to enhance drug loading and prevent drug expulsion during storage. Both systems shown promising results in buccal drug delivery.[15,16]

4.4 Dendrimers

Dendrimers are highly branched, three-dimensional polymeric structures with a high degree of surface functionality. Their unique architecture allows precise control over size and surface charge, making them suitable for targeted and controlled drug delivery via the buccal route.

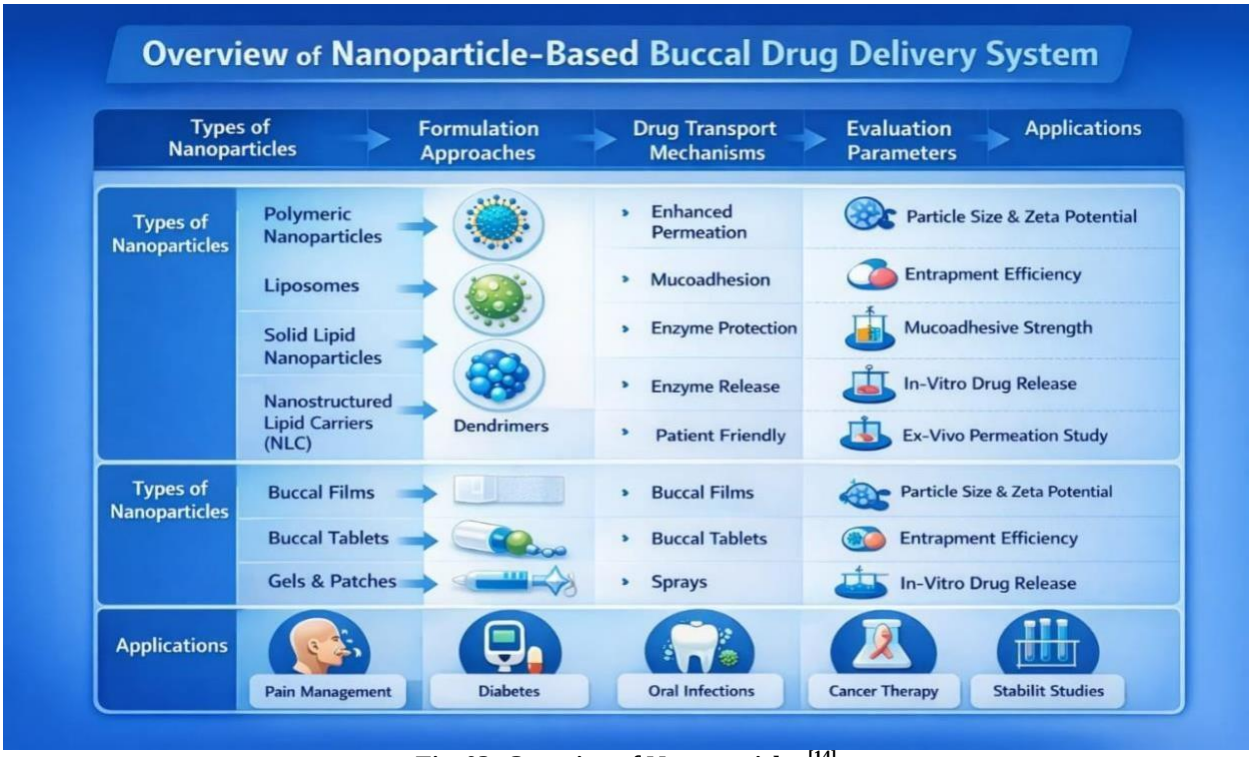

Fig. 02: Overview of Nanoparticles.[14]

5. Formulation Strategies for Nanoparticle-Based Buccal Systems

Nanoparticles are rarely administered alone and are usually incorporated into suitable buccal dosage forms such as films, tablets, gels, and patches. Buccal films are particularly preferred due to their flexibility, ease of application, and patient acceptability. The selection of polymers and excipients plays a critical role in determining mucoadhesion, drug release, and stability of the formulation. Mucoadhesive polymers such as chitosan, Carbopol, hydroxypropyl methylcellulose (HPMC), and sodium alginate are commonly used to enhance retention at the buccal site. The combination of nanoparticles with mucoadhesive matrices provides synergistic benefits in improving drug bioavailability.[17.18,19]

6. Evaluation of Nanoparticle-Based Buccal Drug Delivery Systems

Comprehensive evaluation is essential to ensure the safety, efficacy, and quality of nanoparticle- based buccal formulations. Key parameters include particle size, zeta potential, drug entrapment efficiency, and in-vitro drug release. These parameters influence stability, permeation, and therapeutic performance. Ex-vivo permeation studies using animal buccal mucosa are commonly conducted to assess drug transport across the membrane. Mucoadhesive strength, surface pH, and stability studies are also performed to predict in-vivo performance and shelf life of the formulation.[20,21]

7. Advantages and Limitations

Nanoparticle-based buccal drug delivery systems offer several advantages including avoidance of first-pass metabolism, improved bioavailability, controlled drug release, and enhanced patient compliance. These systems are particularly useful for drugs with poor oral bioavailability and narrow therapeutic windows. these advantages, certain limitations persist such as limited absorption surface area, potential mucosal irritation, and challenges in large-scale manufacturing. Regulatory and stability concerns also need to be addressed before commercial application.[22,23]

8. Future Prospects

Advances in material science and nanotechnology are expected to further improve buccal drug delivery systems. The development of stimuli-responsive nanoparticles and personalized medicine approaches may revolutionize buccal drug administration. Integration of computational modeling and artificial intelligence in nanoparticle design may enhance formulation optimization and therapeutic outcomes.[24,25]

9. CONCLUSION

Nanoparticle-based buccal drug delivery systems represent a promising and innovative approach to

overcoming the limitations of conventional drug delivery routes. By enhancing drug solubility, stability, mucoadhesion, and controlled release, nanoparticles significantly improve therapeutic efficacy and patient compliance. Although challenges remain, continuous research and technological advancements are likely to establish nanoparticle-based buccal systems as a viable platform for future pharmaceutical applications.[26]

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