MANTECH Publications

Journal of Pharmaceutical Chemistry and Drug formulation
Volume 4, Issue 3, September-December, 2022

Formulation of Buccal and Sublingual Drug Delivery Systems: Enhancing Therapeutic Efficacy through Mucosal Administration

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ABSTRACT

Buccal and sublingual drug delivery systems (BDDS and SDDS) provide non-invasive routes for rapid drug absorption and improved bioavailability, bypassing the first-pass metabolism associated with oral administration. These systems are particularly useful for drugs requiring rapid onset of action or those with poor gastrointestinal stability. This paper reviews the formulation strategies, excipient selection, and design considerations for buccal and sublingual drug delivery. Factors affecting mucoadhesion, drug release, and permeation are discussed. Comparative analysis of various dosage forms, including films, tablets, and lozenges, is presented. Stability, patient compliance, and clinical applications are evaluated, emphasizing the role of BDDS and SDDS in enhancing therapeutic outcomes and enabling patient-centric medication.

Keywords: *Buccal drug delivery, Sublingual drug delivery, Mucoadhesive systems, Rapid absorption, Bioavailability, Films, Tablets, Mucosal permeation.*

INTRODUCTION

Oral administration remains the most common route for drug delivery, yet it is limited by first-pass metabolism, gastrointestinal degradation, and variable absorption. Buccal and sublingual drug delivery systems (BDDS and SDDS) offer an alternative by facilitating drug absorption through the oral mucosa directly into systemic circulation. These routes provide rapid onset, improved bioavailability, and enhanced patient compliance. BDDS are applied to the inner cheek, allowing prolonged residence time and controlled release, while SDDS administered under the tongue favor rapid dissolution and absorption. This paper reviews current strategies in formulating effective buccal and sublingual drug delivery systems, including material selection, design, characterization, and clinical relevance.

CLASSIFICATION OF BUCCAL AND SUBLINGUAL DOSAGE FORMS

Dosage Form	Description	Advantages
Buccal Tablets	Compressed tablets applied to the buccal mucosa	Sustained release, prolonged residence time
Sublingual Tablets	Fast-dissolving tablets placed under the tongue	Rapid onset, high bioavailability
Mucoadhesive Films	Thin polymeric films adhering to oral mucosa	Flexible, comfortable, sustained release
Lozenges and Troches	Solid dosage forms dissolving in saliva	Patient-friendly, easy to administer
Patches	Transmucosal adhesive systems	Controlled release, reduced dosing frequency

FORMULATION STRATEGIES Excipients Selection:

- **Mucoadhesive Polymers:** Hydroxypropyl methylcellulose (HPMC), Carbopol, Polyvinyl alcohol (PVA) enhance adhesion and prolong contact time.
- **Permeation Enhancers:** Bile salts, surfactants, fatty acids increase mucosal absorption.
- **Plasticizers:** Glycerin, polyethylene glycol improve film flexibility and patient comfort.
- **Sweeteners and Flavors:** Mask bitter taste and improve patient compliance.

Design Considerations:

- **Drug Solubility and Stability:** Ensure compatibility with polymers and stability in saliva.
- **Drug Release Profile:** Immediate release for SDDS; sustained release for BDDS.
- **Mechanical Properties:** Adequate hardness, flexibility, and mucoadhesion.
- **Patient Acceptability:** Size, taste, and ease of administration are critical.

CHARACTERIZATION TECHNIQUES

- **Thickness and Weight Uniformity:** Ensures consistent dosing.
- **Surface pH:** Prevents mucosal irritation.
- **Swelling Index:** Correlates with mucoadhesion and drug release.
- **Mucoadhesive Strength:** Measured using texture analyzer or detachment force studies.
- **In Vitro Dissolution Studies:** Assess drug release kinetics.
- **Ex Vivo Permeation Studies:** Buccal or sublingual mucosa models to evaluate absorption.

COMPARATIVE ANALYSIS OF BUCCAL AND SUBLINGUAL SYSTEMS

Parameter	Buccal	Sublingual
Onset of Action	Moderate (sustained release)	Rapid (immediate release)
Residence Time	Longer (up to 12 h)	Shorter (minutes to 1 h)
Bioavailability	Enhanced by bypassing first-pass	Highly enhanced, rapid peak plasma levels
Patient Compliance	Requires careful placement	Easy, more acceptable for children and elderly
Suitable Drugs	Peptides, hormones, antiemetics	Cardiovascular drugs, analgesics, nitrates

CASE STUDIES

Nitroglycerin Sublingual Tablets: Rapid relief in angina pectoris due to fast absorption and bypass of hepatic metabolism.

Buserelin Buccal Tablets: Prolonged release hormone therapy for reproductive disorders; mucoadhesive polymers enhance residence time.

Fentanyl Buccal Films: Controlled opioid release for pain management; flexible, patient-friendly, and rapid onset.

STABILITY AND REGULATORY CONSIDERATIONS

- **Chemical Stability:** Drug-polymer interactions and saliva pH may affect stability.
- **Physical Stability:** Moisture uptake, film brittleness, and tablet hardness must be controlled.
- **Regulatory Compliance:** Dosage uniformity, content validation, and safety studies are essential.
- **Packaging:** Protective blister packs or sachets to maintain integrity and prevent moisture damage.

ADVANTAGES OF BUCCAL AND SUBLINGUAL DELIVERY

1. **Bypass First-Pass Metabolism:** Increases bioavailability for drugs extensively metabolized in the liver.
2. **Rapid Onset of Action:** Particularly important for cardiovascular emergencies and analgesics.
3. **Improved Patient Compliance:** Non-invasive, easy to administer, suitable for pediatrics and geriatrics.
4. **Controlled and Sustained Release:** Buccal systems enable extended therapeutic effects.
5. **Reduced Systemic Side Effects:** Localized delivery minimizes systemic exposure.

FUTURE PERSPECTIVES

- **Integration with Nanotechnology:** Liposomes, nanoparticles, and nanoemulsions for enhanced permeation and targeted delivery.
- **Personalized Medicine:** Tailored buccal/sublingual formulations based on patient pharmacogenomics.
- **Smart Mucoadhesive Systems:** pH-responsive or enzyme-triggered drug release.
- **Digital Health Integration:** Patient adherence monitoring via smart patches or films.
- **Expansion to Biologics:** Delivery of peptides, proteins, and vaccines through oral mucosa.

CONCLUSION

Buccal and sublingual drug delivery systems provide effective non-invasive alternatives to conventional oral administration, enabling rapid onset, improved bioavailability, and enhanced patient compliance. Formulation strategies focusing on mucoadhesive polymers, permeation enhancers, and appropriate dosage forms ensure optimal drug absorption and therapeutic efficacy. Characterization techniques, stability considerations, and regulatory compliance are critical for successful development. Case studies of nitroglycerin, buserelin, and fentanyl illustrate the clinical relevance of BDDS and SDDS. Future integration with nanotechnology, smart materials, and personalized medicine is expected to expand the applications and effectiveness of buccal and sublingual drug delivery, establishing these systems as pivotal tools in modern pharmaceutics.

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