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Development of Buccal Patches Using Quality by Design

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Abstract: The introduction of pharmacotherapy with macromolecules, including peptides, proteins, polysaccharides, and nucleic acids, has revolutionized modern pharmacotherapy because of their highly site-specific action and excellent toxicity profiles. Despite their superior pharmacological effectiveness, macromolecular agents are faced with critical delivery challenges that seriously limit their clinical applications. Considerable pre systemic elimination, acidic digestive degradation of the stomach, and poor oral bioavailability pose significant barriers to effective therapeutic response. More conventional methods of parenteral administration, while eliminating GI barriers, impose disadvantages like high cost, poor patient compliance, frequent administration, and complications associated with invasive therapy. Buccal patch technology has emerged as a novel alternative delivery platform designed to overcome these formulation challenges. Positioned between the upper gingiva and the buccal mucosa, these patches allow for drug absorption through highly permeable buccal mucosa. The main advantage of this route is direct access to the systemic circulation through the internal jugular vein, thereby avoiding hepatic first-pass metabolism and significantly improving the bioavailability. The buccal mucosa presents ideal characteristics for drug delivery, such as easy accessibility, high permeability, and rich vascularity, thus making it suitable for both topical and systemic active applications. Application of (QbD) principles in the development of buccal patches offers an avenue for systematic optimization and scientific rigor during formulation. The approach starts with the definition of QTPP, which is followed by systematic identification of critical quality attributes, including mucoadhesive strength, drug content uniformity, surface pH, and controlled-release characteristics. Careful optimization of CMAs and CPPs allows product developers to achieve consistent product quality, enhanced bioavailability, and superior therapeutic efficacy while adhering to regulatory compliance. It also covers some of the basic aspects of buccal patch technology: anatomy and physiology of buccal mucosa, mechanisms of drug permeation, theories governing mucoadhesion, formulation design strategies, and standardized protocols for its evaluation. The amalgamation of QbD principles with buccal delivery technology offers a sound basis for the development of patient-friendly, efficient therapeutic systems for macromolecular drugs. This constitutes a meaningful advance in transmucosal drug delivery because of its

better bioavailability, improved therapeutic response, and outstanding reproducibility that positions buccal patches for future pharmaceutical delivery systems.

Keywords: Buccal patches, mucoadhesive drug delivery, first-pass metabolism, bioavailability enhancement, trans mucosal absorption, macromolecular drugs.

INTRODUCTION

The pharmaceutical industry has witnessed remarkable advancements in drug discovery and development over the past few decades, resulting in the identification and synthesis of numerous therapeutically active compounds with immense potential to treat a wide array of diseases. However, the clinical success of any pharmaceutical agent is not solely dependent on its inherent pharmacological activity but is equally contingent upon the efficiency with which it can be delivered to its site of action at therapeutically relevant concentrations. The route of drug administration plays a pivotal role in determining the ultimate therapeutic outcome, influencing not only the rate and extent of drug absorption but also its bioavailability, distribution, metabolism, and elimination profile.

Among the various routes of drug administration available to clinicians and patients, the oral route has traditionally been, and continues to be, the most preferred and widely utilized method of drug delivery. This preference stems from several inherent advantages that make oral administration particularly attractive from both clinical and patient perspectives. The oral route offers unparalleled convenience, eliminating the need for trained healthcare professionals for drug administration and allowing patients to self-administer medications in the comfort of their homes. It is non-invasive, thereby avoiding the pain, anxiety, and potential complications associated with needle-based delivery systems. The oral route generally demonstrates excellent patient compliance due to its ease of use and social acceptability. Furthermore, oral formulations are typically more cost-effective to manufacture, store, and distribute compared to sterile parenteral preparations, making them economically advantageous for both pharmaceutical manufacturers and healthcare systems.

Despite these numerous advantages, conventional peroral drug administration—wherein medications are swallowed and absorbed primarily through the gastrointestinal tract—is associated with several significant and often insurmountable limitations that can severely compromise therapeutic efficacy for certain classes of drugs. Chief among these limitations is the extensive hepatic first-pass metabolism, a phenomenon wherein drugs absorbed from the gastrointestinal tract are transported via the portal circulation directly to the liver before entering the systemic circulation. In the liver, many drugs undergo extensive biotransformation by phase I and phase II metabolic enzymes, resulting in a substantial reduction in the amount of parent drug that ultimately reaches the systemic circulation and target tissues. For drugs with high hepatic extraction ratios, this first-pass effect can reduce bioavailability to such an extent that therapeutic concentrations become difficult or impossible to achieve through oral administration alone.

In recognition of these fundamental limitations of conventional oral drug delivery, pharmaceutical scientists and researchers have devoted considerable effort to exploring and developing alternative routes of administration that can circumvent the barriers imposed by the gastrointestinal tract and hepatic first-pass metabolism. Among these alternatives, transmucosal drug delivery routes have emerged as particularly promising platforms for systemic drug administration. Trans mucosal routes exploit the absorptive capacity of various mucous membranes lining body cavities and passages, including the nasal mucosa, rectal mucosa, vaginal mucosa, ocular mucosa, and the diverse mucosal surfaces of the oral cavity. These mucosal surfaces possess several advantageous characteristics that make them attractive for drug delivery applications.

The fundamental advantages offered by trans mucosal routes over conventional peroral administration are multifaceted and clinically significant. First and foremost, drugs absorbed

through most mucosal membranes can gain direct access to the systemic circulation, completely bypassing the hepatic portal system and thereby avoiding first-pass hepatic metabolism. This bypass mechanism can dramatically enhance the bioavailability of drugs that would otherwise be extensively metabolized during their first passage through the liver. Second, trans mucosal routes avoid the harsh enzymatic environment of the gastrointestinal tract, protecting acid-labile and enzyme-susceptible drugs from degradation and enabling the delivery of peptides, proteins, and other biologics that would be destroyed if administered orally. Third, depending on the specific drug and the particular mucosal site, the enzymatic flora and metabolic activity at mucosal surfaces may be more favourable for drug stability and absorption compared to the gastrointestinal tract. Fourth, many mucosal surfaces are highly vascularized, facilitating rapid drug absorption and onset of action. Finally, trans mucosal routes may offer opportunities for sustained or controlled drug release through the use of mucoadhesive delivery systems that can maintain prolonged contact between the formulation and the absorbing membrane.

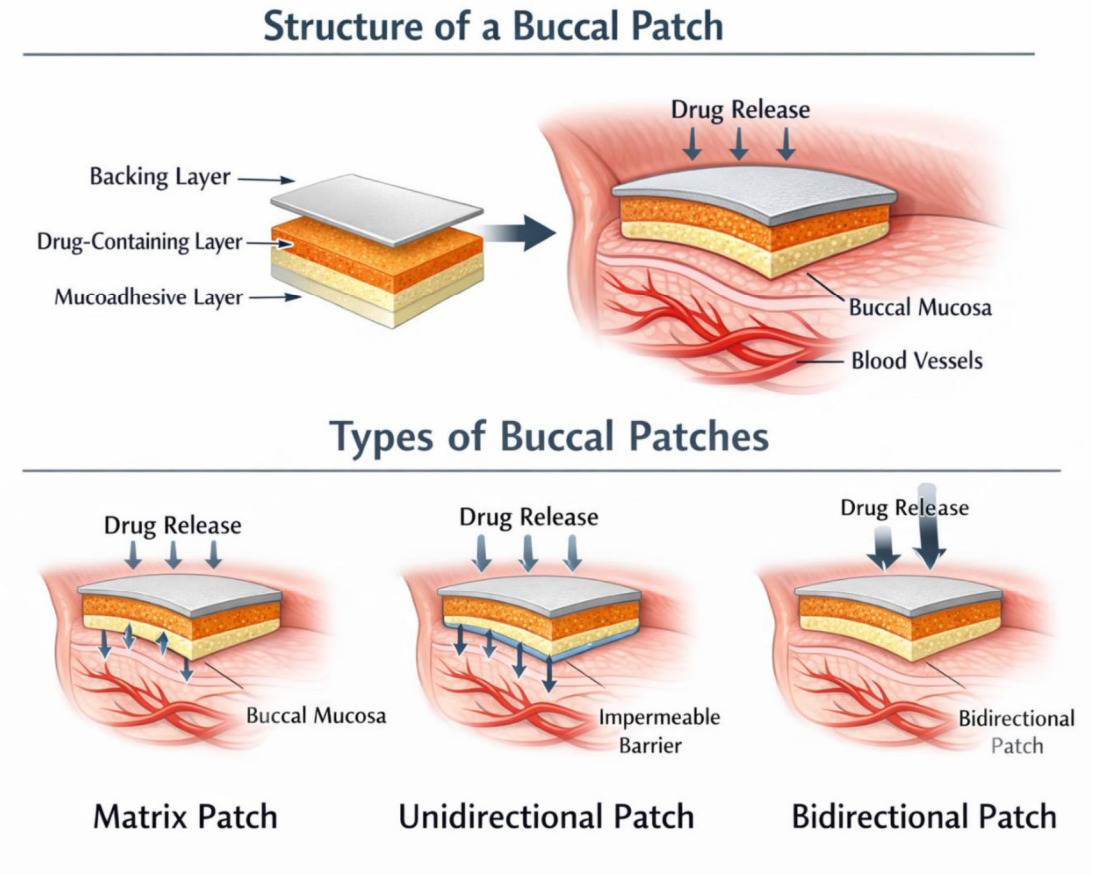

Figure 1 & 2

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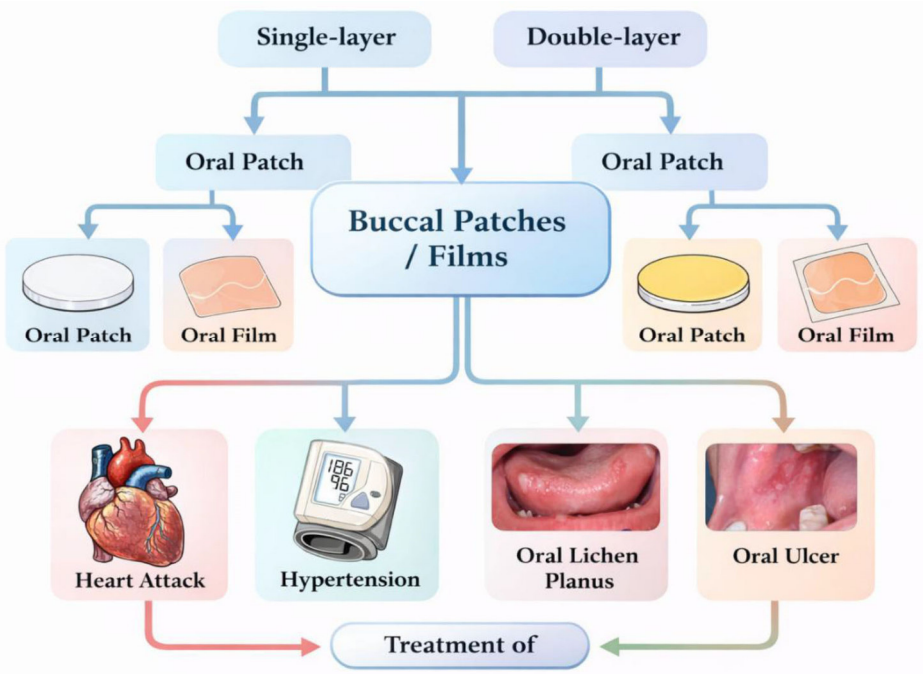

Figure 3

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Drugs absorbed through the buccal mucosa gain direct entry into the systemic circulation via the facial vein, which drains into the internal jugular vein, thereby completely circumventing hepatic first-pass metabolism. This unique anatomical arrangement enables the achievement of significantly higher systemic bioavailability for drugs that would otherwise be extensively metabolized during their first passage through the liver. Additional advantages of the buccal route include excellent accessibility for placement and removal of dosage forms, painless administration that promotes patient compliance, relatively low inter-individual variability in absorption compared to nasal or rectal routes, the ability to easily terminate drug delivery by removing the dosage form in case of adverse effects, and the versatility to design drug delivery systems that can target either local therapeutic effects within the oral cavity or systemic therapeutic effects throughout the body.

Buccal patches offer several critical advantages over other mucoadhesive dosage forms, particularly gel-based formulations. While gels can be easily applied and spread over mucosal surfaces, they suffer from the fundamental limitation of having relatively short residence times on the mucosa due to their susceptibility to dilution, displacement, and washout by saliva flow. The continuous secretion of saliva in the oral cavity—typically ranging from 0.5 to 2 liters per day—creates a dynamic aqueous environment that rapidly dilutes and removes gel formulations, limiting their effectiveness for sustained drug delivery. In contrast, buccal patches, by virtue of their solid structure and strong mucoadhesive properties, can resist salivary washout and maintain their position and integrity throughout the intended delivery period, which may range from several hours to even days depending on the formulation design.

Furthermore, buccal patches provide patients with greater comfort and freedom compared to other devices. Unlike bulky tablets or disks that may cause discomfort, interfere with speech and eating, or generate foreign body sensations, properly designed patches are thin, flexible, and virtually imperceptible once applied, allowing patients to carry out normal daily

activities including speaking, eating, and drinking with minimal interference. The discrete nature of patches also enhances patient acceptability and compliance, particularly for medications that must be administered in social or professional settings where visible or obtrusive delivery devices might cause embarrassment or inconvenience.

From a technical and formulation perspective, buccal patches offer pharmaceutical developer remarkable versatility in design options. Patches can be formulated with impermeable backing layers to control the direction of drug release, with permeation enhancers to improve drug flux across the mucosa, with enzyme inhibitors to protect peptide and protein drugs from degradation, with pH modifiers to optimize drug solubility and stability, and with various mucoadhesive polymers selected to achieve desired adhesion strength and duration. This design flexibility enables the development of sophisticated, multifunctional drug delivery systems optimized for specific therapeutic applications and patient needs.

Types of Buccal Patches

1. Based on Structural Design
2. Based on Release Mechanism
3. Based on Physical Form
4. Based on Functional Characteristics
5. Based on Drug Loading
6. Novel Types

1. Based on Structural Design

Monolayer Patches: These consist of a single layer containing the drug, polymer, and other excipients in a homogeneous mixture. They are simple to fabricate but offer limited control over drug release direction and may allow drug loss through saliva.

Bilayer Patches: These patches comprise two distinct layers: a drug-containing mucoadhesive layer that contacts the buccal mucosa, and a backing layer that provides structural support and prevents drug loss toward the buccal cavity. The backing layer is typically impermeable and protects the patch from saliva washout.

Multilayer Patches: These sophisticated systems contain three or more layers, often incorporating rate-controlling membranes between the drug reservoir and mucoadhesive layer. They offer precise control over drug release kinetics and directional delivery.

2. Based on Release Mechanism

Matrix-Type Patches: The drug is uniformly dispersed throughout the polymer matrix. Release occurs through diffusion as the polymer hydrates and swells. These are simple to manufacture and provide sustained release, though release rate decreases over time as the diffusion path lengthens.

Reservoir-Type Patches: The drug is contained in a central reservoir surrounded by a rate-controlling membrane. This design provides more consistent zero-order release kinetics compared to matrix systems, maintaining steady drug levels throughout the delivery period.

Gradient-Type Patches: These contain varying drug concentrations across different layers or zones, designed to maintain optimal drug concentration gradients for enhanced permeation through the buccal mucosa.

3. Based on Physical Form

Adhesive Patches: These rely on mucoadhesive polymers that form intimate contact with the mucosal surface through various bonding mechanisms. They maintain position through adhesive forces without mechanical retention.

Non-Adhesive Patches: Less common, these systems may use mechanical retention methods or are designed for short-term application where adhesion is not critical.

4. Based on Functional Characteristics

Immediate-Release Patches: Designed for rapid drug delivery, these patches disintegrate or release their contents quickly upon contact with buccal fluids, suitable for acute symptom management.

Sustained/Controlled-Release Patches: These provide prolonged drug delivery over extended periods (hours to days), maintaining therapeutic drug levels and reducing dosing frequency. They employ various mechanisms including polymer erosion, diffusion, and osmotic pressure.

Mucoadhesive Patches: Specifically formulated with polymers that adhere strongly to the mucosa, ensuring prolonged residence time and enhanced drug absorption. Common polymers include chitosan, carbopol, hydroxypropyl methylcellulose (HPMC), and sodium alginate.

Bio-erodible Patches: These gradually dissolve or erode in the buccal environment, eliminating the need for patch removal. The erosion rate is designed to match the desired drug release profile.

5. Based on Drug Loading

Drug-in-Adhesive Patches: The active pharmaceutical ingredient is incorporated directly into the adhesive layer, simplifying manufacturing and providing a thin profile.

Drug-in-Matrix Patches: The drug is dispersed within a separate polymer matrix layer, distinct from the adhesive component, allowing independent optimization of adhesion and release properties.

6. Advanced/Novel Types

Microemulsion-Based Patches: Incorporate micro emulsions to enhance solubility and permeation of poorly water-soluble drugs.

Nanoparticle-Loaded Patches: Contain drug-loaded nanoparticles (polymeric, lipid-based, or inorganic) for targeted delivery, protection of sensitive drugs, and enhanced permeation.

Hydrogel-Forming Patches: Transform into hydrogels upon contact with mucosal fluids, providing comfortable wear and controlled drug release through the gel network.

Stimulus-Responsive Patches: Smart systems that respond to specific triggers such as pH, temperature, or enzymatic activity in the buccal environment to modulate drug release.

The selection of patch type depends on the specific drug characteristics, desired release profile, duration of therapy, patient comfort requirements, and manufacturing feasibility. Modern buccal patch development often combines features from multiple categories to create optimized delivery systems tailored to specific therapeutic needs.

Introduction to Quality by Design (QbD)

Quality by Design (QbD) is a systematic, science-based approach to pharmaceutical development that focuses on building quality into a product from the very beginning rather than relying only on end-product testing. It involves a thorough understanding of the drug, excipients, and manufacturing process, along with the identification and control of factors that can affect product quality. By using tools such as risk assessment and design of experiments, QbD helps ensure consistent product performance, safety, and efficacy. Regulatory agencies like the USFDA and ICH encourage the adoption of QbD as it reduces formulation failures, improves reproducibility, and supports efficient scale-up. In the development of buccal patches, QbD plays a crucial role in achieving optimal mucoadhesion, uniform drug distribution, controlled drug release, and enhanced patient comfort, making the dosage form more reliable and patient-friendly.

Why QbD Is Important in Pharmaceuticals

Traditional formulation follows a **trial-and-error approach**, which may lead to:

- Batch failures
- Inconsistent quality
- Scale-up problems

QbD overcomes these issues by:

- Understanding the product and process deeply
- Identifying critical variables early
- Reducing development time and cost
- Ensuring consistent product quality

Where QbD Is Used

QbD is widely used in:

- Tablet and capsule formulation
- Transdermal and buccal patches
- Novel drug delivery systems
- Controlled and sustained release dosage forms
- Scale-up and technology transfer

It is especially useful where **multiple formulation and process variables** influence product performance.

How QbD Is Used

1. Decide what the final product should be (QTPP)
2. Identify important quality parameters (CQAs)
3. Study drug and excipient properties (CMAs)
4. Identify risky steps using risk assessment
5. Optimize variables using DoE

6. Define design space
7. Apply control strategy

This makes formulation development **predictable and reproducible**.

Why QbD Is Helpful for Buccal Patches

Buccal patches are **sensitive dosage forms** because:

- They come in direct contact with oral mucosa
- Small changes can affect adhesion and drug release
- Patient comfort is very important

QbD helps overcome these challenges effectively.

Role of QbD in Buccal Patch Development

1. Improves Mucoadhesion

By optimizing polymer type and concentration, QbD ensures:

- Adequate adhesion to buccal mucosa
- Longer residence time
- Reduced patch detachment

2. Ensures Uniform Drug Distribution

QbD controls mixing, casting, and drying parameters, resulting in:

- Uniform drug content
- Reduced dose variation

3. Controls Drug Release

Through systematic optimization, QbD helps achieve:

- Desired release pattern (immediate or controlled)
- Predictable therapeutic effect

4. Enhances Patient Compliance

Optimized thickness, flexibility, and surface pH make the patch:

- Comfortable to wear
- Non-irritant
- Easy to remove

Advantages of QbD for Buccal Patches

- Reduces formulation failures
- Ensures batch-to-batch consistency
- Saves time and cost
- Improves regulatory acceptance
- Makes scale-up easier

METHODS OF PREPARATION

Methods of Preparation of Buccal Patches

1. Solvent Casting Method
2. Direct Compression Method
3. Hot Melt Extrusion Method
4. Semisolid Casting Method
5. Freeze-Drying (Lyophilization) Method

1. Solvent Casting Method

This is the **most commonly used method** for preparing buccal patches.

In this method, the drug and muco-adhesive polymers are dissolved in a suitable solvent such as water, ethanol, or a mixture of solvents. Plasticizers like glycerol or PEG are added to improve flexibility. The clear solution is poured into a mould or petri dish and allowed to dry at room temperature or in a controlled oven. After complete drying, the formed film is carefully peeled off and cut into patches of the required size.

Advantages:

- Simple and economical
- Uniform drug distribution
- Suitable for heat-sensitive drugs

2. Direct Compression Method

This method is mainly used when a thicker buccal patch or buccal tablet-type patch is required.

The drug, polymers, and excipients are mixed uniformly in dry form. The powder blend is then compressed using a tablet compression machine with flat punches to obtain buccal patches. No solvent is used in this method.

Advantages:

- Solvent-free process
- Short preparation time
- Good mechanical strength

3. Hot Melt Extrusion Method

In this method, the drug is mixed with thermoplastic polymers and heated until it forms a molten mass. The molten mixture is passed through an extruder to form thin films. After cooling, the films are cut into required patch sizes.

Advantages:

- No use of solvents
- Continuous and scalable process
- Suitable for controlled drug release

Limitation:

- Not suitable for heat-sensitive drugs

4. Semisolid Casting Method

This method is used when **acid-insoluble polymers** are involved.

First, a solution of water-soluble polymers is prepared. Separately, acid-insoluble polymers are dissolved in an organic solvent. Both solutions are mixed to form a viscous semisolid mass. This mass is then cast onto a flat surface and dried to form buccal patches.

Advantages:

- Good film uniformity
- Suitable for multilayer patches

5. Freeze-Drying (Lyophilization) Method

In this method, the drug and polymer are dissolved in water to form a solution. The solution is poured into moulds and frozen at very low temperatures. The frozen solvent is then removed by sublimation using a freeze dryer, resulting in a porous buccal patch.

Advantages:

- Highly porous structure
- Rapid drug release
- Improved patient comfort

QbD-Based Methods of Preparation of Buccal Patches

1. Defining Quality Target Product Profile (QTPP)
2. Identification of Critical Quality Attributes (CQAs)
3. Selection of Drug and Excipients (CMAs)
4. Risk Assessment (QbD Tools)
5. Optimization Using Design of Experiments (DoE)
6. QbD-Based Solvent Casting Preparation
7. Control Strategy and Product Evaluation

1. Defining Quality Target Product Profile (QTPP)

QTPP is the **first and most important step** in QbD. It clearly defines what the buccal patch is expected to achieve.

In buccal patch development, QTPP includes:

- Type of delivery (local or systemic)
- Dosage form (mucoadhesive buccal patch)
- Drug release pattern (immediate or controlled)
- Residence time on buccal mucosa
- Patient comfort and safety

This step acts as a **blueprint** for the entire formulation process.

2. Identification of Critical Quality Attributes (CQAs)

CQAs are the **measurable quality parameters** that must be controlled to meet QTPP. For buccal patches, important CQAs include:

- Drug content uniformity
- Patch thickness and weight variation
- Mucoadhesive strength
- Folding endurance
- Surface pH
- In-vitro drug release

Any variation in these attributes can affect patch performance.

3. Selection of Drug and Excipients (CMAs)

Critical Material Attributes (CMAs) refer to the **properties of drug and excipients** that influence CQAs.

Selection is done based on:

- Drug solubility and permeability
- Compatibility with polymers
- Mucoadhesive polymer type (HPMC, Carbopol, PVA, etc.)
- Plasticizer concentration for flexibility

QbD ensures rational selection instead of trial-and-error.

4. Risk Assessment (QbD Tools)

Risk assessment helps identify critical formulation and process variables.

Commonly used tools:

- Ishikawa (Fish-bone) diagram
- Failure Mode and Effects Analysis (FMEA)

High-risk factors may include:

- Polymer concentration
- Drying temperature
- Mixing time

This step minimizes formulation failures.

5. Optimization Using Design of Experiments (DoE)

DoE is used to study the effect of multiple variables simultaneously.

Typical factors studied:

- Polymer concentration
- Plasticizer level
- Drying time

Responses measured:

- Mucoadhesive strength

- Drug release
- Mechanical properties

DoE helps establish an optimized formulation with minimum experiments.

6. QbD-Based Solvent Casting Preparation

After optimization, the buccal patches are prepared using a controlled solvent casting method.

The drug and polymers are dissolved in a suitable solvent under controlled stirring. Optimized plasticizer concentration is added. The solution is cast onto a mould and dried under predefined temperature and time (within the design space). The dried film is cut into uniform patches.

QbD ensures **batch-to-batch consistency** and reproducibility.

7. Control Strategy and Product Evaluation

A control strategy is implemented to ensure consistent quality.

Includes:

- In-process checks (thickness, weight)
- Final evaluation (drug content, folding endurance, mucoadhesion, release study)

This step confirms that the buccal patch meets **all QTPP and CQAs**

Marketed Buccal Patch

Table 1

Product Name	Active Ingredient	Type/Form	Indication (Therapeutic Use)	Application Site
Belbuca®	Buprenorphine	Buccal film	Management of chronic pain (opioid analgesic)	Buccal mucosa (inner cheek)
Bunavail®	Buprenorphine + Naloxone	Buccal film	Opioid dependence (maintenance therapy)	Buccal mucosa
Suboxone® (buccal film)	Buprenorphine + Naloxone	Buccal film	Opioid use disorder	Buccal mucosa
Onsolis®	Fentanyl	Buccal soluble film	Breakthrough cancer pain	Buccal mucosa
Lorenzo® *(brand example varies)*	Lidocaine / Benzocaine	Buccal patch/film	Oral pain relief / anesthesia	Buccal mucosa (pain areas)
OraDisc® *(OTC)*	Various analgesics	Buccal/Oral patches	Minor oral discomfort relief	Buccal/oral mucosa
Mucotrol®	Hyaluronic acid / soothing agents	Buccal adhesive patch	Soothe oral ulcers / mucosal lesions	Affected buccal mucosa
Striant®	Testosterone	Buccal mucoadhesive tablet/patch	Testosterone replacement therapy	Upper gum / buccal mucosa
Nitrostat® *(buccal alternative form)*	Nitro-glycerine	Buccal / sublingual	Angina (rapid vasodilator)	Buccal/sublingual area
Versatis® *(topical patch)*	Lidocaine 5%	Patch applied near facial/oral pain areas	Post-herpetic neuralgia pain	Near affected mucosa / skin adjacent

Types of Conventional Tablets, Description & Use

Table 2

Type of Tablet	Description / Characteristics	Typical Use / Purpose
Compressed Tablets	Prepared by single compression of drug + excipients	Most common oral dosage form for systemic delivery

Type of Tablet	Description / Characteristics	Typical Use / Purpose
Multiple-Compressed Tablets	Made by more than one compression step (e.g., core + coat)	Drug separation, sustained release, or protection
Sugar-Coated Tablets	Tablet coated with sugar layer for taste masking & protection	Improves palatability and appearance
Film-Coated Tablets	Thin polymer coating applied over tablet	Protection, taste masking, improved stability
Enteric-Coated Tablets	Coating resists gastric acid and dissolves in intestine	Prevents gastric irritation / protects acid-labile drugs
Chewable Tablets	Designed to be chewed before swallowing	Pediatric & geriatric patients, antacids, vitamins
Effervescent Tablets	Contain acid + carbonate → fizz in water before intake	Rapid dissolution, faster absorption
Buccal Tablets	Placed in buccal cavity; slow drug absorption through mucosa	Sustained systemic effect (e.g., hormones, analgesics)
Sublingual Tablets	Placed under tongue for rapid absorption	Emergency / rapid-onset drugs (e.g., nitro-glycerine)
Lozenges / Troches	Dissolve slowly in mouth; local therapeutic effect	Throat infections, oral antifungal / antiseptic delivery
Vaginal Tablets	Intended for insertion into vaginal cavity	Local antimicrobial / antifungal therapy
Implantation Tablets	Sterile tablets placed subcutaneously / intramuscularly	Long-acting hormone / contraceptive / cancer therapy
Dispensing Tablets	High-dose tablets divided by pharmacist for compounding	Rare, used in extemporaneous preparations

CONCLUSION

The emergence of buccal patches as an advanced drug delivery system represents a significant breakthrough in pharmaceutical sciences, offering an elegant solution to the long-standing challenges associated with conventional oral and parenteral drug administration. Traditional oral delivery suffers from extensive hepatic first-pass metabolism, harsh gastro-intestinal enzymatic degradation, and unpredictable bioavailability, particularly limiting the therapeutic potential of macromolecular drugs such as peptides, proteins, and nucleic acids. While parenteral administration circumvents these barriers, it introduces challenges including poor patient compliance, pain, high costs, and risk of infections. Buccal patches ingeniously bridge this therapeutic gap by combining the con-venience of oral administration with enhanced bioavailability, utilizing the buccal mucosa's unique anatomical advantages—rich vascularization with direct drainage into the systemic circulation via the internal jugular vein, com-pletely bypassing hepatic first-pass metabolism and achieving significantly higher drug bioavailability.

The classification of buccal patches into matrix-type (bi-directional) and reservoir-type (uni-directional) reflects thoughtful pharma-ceutical engineering tailored to specific therapeutic needs. Matrix-type patches offer simplicity in manufacturing with homogeneous drug distribution and dual therapeutic action suitable for conditions requiring both local and systemic effects, though they experience some drug loss into saliva. In contrast, reservoir-type patches feature sophisticated multi-layered architecture with impermeable backing layers that maximize systemic bioavailability by directing all drug toward the mucosa, provide superior control over release kinetics, mask unpleasant tastes, and offer enhanced protection for labile molecules. This structural diversity, combined with the ability to incorporate permeation enhancers, enzyme inhibitors, and mucoadhesive polymers, enables pharmaceutical scientists to develop personalized therapeutic solutions addressing unique challenges posed by different drug candidates and clinical scenarios.

Among various mucoadhesive dosage forms—tablets, films, gels, disks, and ointments—buccal patches have distinguished themselves as the most versatile and patient-friendly option due to their resistance to salivary washout, thin and flexible structure ensuring comfort, discrete nature enhancing social acceptability, and ease of removal providing patient control. These patches offer compelling clinical advantages including painless non-invasive administration that enhances compliance, sustained controlled release reducing dosing frequency, and the ability to terminate therapy immediately if adverse reactions occur. The economic benefits are equally significant, as enhanced bioavailability enables dose reductions that offset manufacturing costs, while prevention of drug wastage through uni-directional delivery provides substantial value, particularly for expensive biologics.

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