

## A REVIEW ON FORMULATION AND EVALUATION OF BUCCAL PATCHES OF METRONIDAZOLE FOR THE TREATMENT OF PERIODONTITIS

\*<sup>1</sup>Prachi Dukhande, <sup>2</sup>Ronal Dsilva, <sup>3</sup>Srushti Davari, <sup>4</sup>Roshan Gamare, <sup>5</sup>Ms. Manasi Mathkar

<sup>1,2,3,4</sup>Student, Shree Saraswati Institute of Pharmacy, Tondavali, Kankavli.

<sup>5</sup>Assistant Professor, Shree Saraswati Institute of Pharmacy, Tondavali, Kankavli.

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### \*Corresponding Author

**Prachi Dukhande**

Student, Shree Saraswati Institute of Pharmacy, Tondavali, Kankavli.



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### ABSTRACT

Periodontitis is a chronic inflammatory disease affecting the supporting tissues of the teeth and is mainly caused by bacterial plaque accumulation. Conventional dosage forms used in its treatment may show limitations such as poor bioavailability, frequent dosing, and reduced patient compliance. To overcome these limitations, the present study was aimed at formulating and evaluating a buccal patch of Metronidazole for the treatment of periodontitis. Buccal drug delivery systems provide several advantages such as bypassing first-pass metabolism, improved bioavailability and ease of administration. The buccal patches were prepared by solvent casting method using Hydroxypropyl Methylcellulose (HPMC) as the polymer and glycerine as the plasticizer. Different formulations (F1–F5) were developed with varying

concentrations of polymers and excipients. Prefor mulation studies of metronidazole including physical appearance, solubility, melting point, and UV calibration curve were carried out. The prepared patches were further evaluated for parameters such as weight uniformity, thickness, folding endurance, surface pH, moisture content, etc., The evaluation results indicated that all formulations showed satisfactory physicochemical properties and acceptable performance. Among all formulations, batch F3 exhibited better weight uniformity, optimum thickness, maximum folding endurance, and suitable surface pH, indicating good flexibility and compatibility with buccal mucosa. The study concluded that

metronidazole buccal patches are a promising and effective drug delivery system for localized treatment of periodontitis with improved patient compliance.

**KEYWORDS:** Metronidazole, Buccal Patch, Periodontitis, HPMC, Solvent Casting Method.

## INTRODUCTION

In recent years, considerable research has been focused on the development of advanced drug delivery systems that can target specific sites in the body, with the aim of improving drug bioavailability and minimizing dose-related side effects.<sup>[1]</sup> Among the various novel approaches, the buccal drug delivery system has gained significant attention as a promising alternative to conventional routes of drug administration. This is mainly because the buccal mucosa is highly permeable and possesses a rich blood supply, which facilitates efficient drug absorption. Drugs administered through the buccal route directly enter the systemic circulation, thereby bypassing first-pass metabolism in the liver and avoiding degradation in the harsh gastrointestinal environment. In addition, the buccal cavity is easily accessible, which allows for simple and convenient self-administration, improving patient compliance.<sup>[2]</sup>

This route becomes particularly important in the management of oral conditions such as periodontitis. Periodontitis is highly prevalent worldwide, affecting approximately 40–50% of adults, while severe forms are observed in about 10–15% of the population. In India, the prevalence is even higher, with nearly 60–70% of adults being affected. The occurrence of periodontitis increases with age and is more commonly seen in individuals above 30 years.<sup>[3]</sup>

In this context, buccal patches offer a suitable and advantageous approach for the management of such conditions. Buccal patches are thin, flexible dosage forms that can be easily applied to the buccal mucosa, allowing controlled and sustained release of the drug. They are simple to use, can be easily removed if required, and provide better control over drug delivery. Additionally, they offer improved patient compliance and flexibility compared to many conventional dosage forms. Thus, the buccal drug delivery system, particularly in the form of buccal patches, represents an effective and promising strategy for the management of periodontitis.<sup>[4,5]</sup>

## INTRODUCTION TO DISEASE

Periodontitis is a long-term inflammatory disease that affects the supporting structures of the teeth, such as gums and bone. It is mainly caused by the buildup of dental plaque containing

harmful bacteria. If gingivitis is not treated, it can progress into periodontitis, leading to damage of the surrounding tissues. Common symptoms include bleeding gums, swelling, bad breath, gum recession, and loosening of teeth in severe cases.<sup>[6]</sup>

The disease occurs due to the interaction between bacteria and the body's immune response, which results in destruction of gum tissue and bone. Factors like poor oral hygiene, smoking, diabetes, and genetic conditions can increase the risk of periodontitis. It can be classified into different types based on its severity and progression.

Diagnosis is done by clinical examination and measuring gum pocket depth. Treatment mainly includes proper oral hygiene, scaling and root planning, and sometimes the use of medicines or surgery. Although the damage caused cannot be completely reversed, early treatment can control the disease and prevent further complications.<sup>[7,8]</sup>

### **BUCCAL PATCH**

A buccal patch is a thin polymeric film that adheres to the buccal mucosa and releases the drug in a controlled manner. The patch gradually dissolves or erodes after administration. It is made of one or more layers of polymer films that contain the drug along with other ingredients. The patch usually has a mucoadhesive layer that helps it stick to the oral mucosa, gums, or teeth. This allows the drug to be released in a controlled manner either into the oral mucosa, the oral cavity, or both.<sup>[9]</sup>

### **Manufacturing methods of buccal patches/ films<sup>[10]</sup>**

1. Solvent Casting Method
2. Direct Milling Method
3. Hot Melt Extrusion Method
4. Semisolid Casting Method
5. Solid Dispersion Method

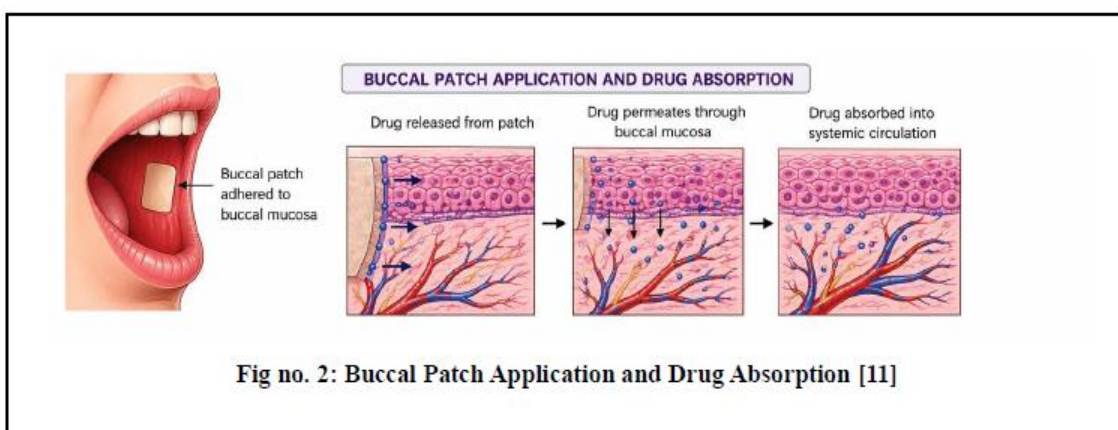
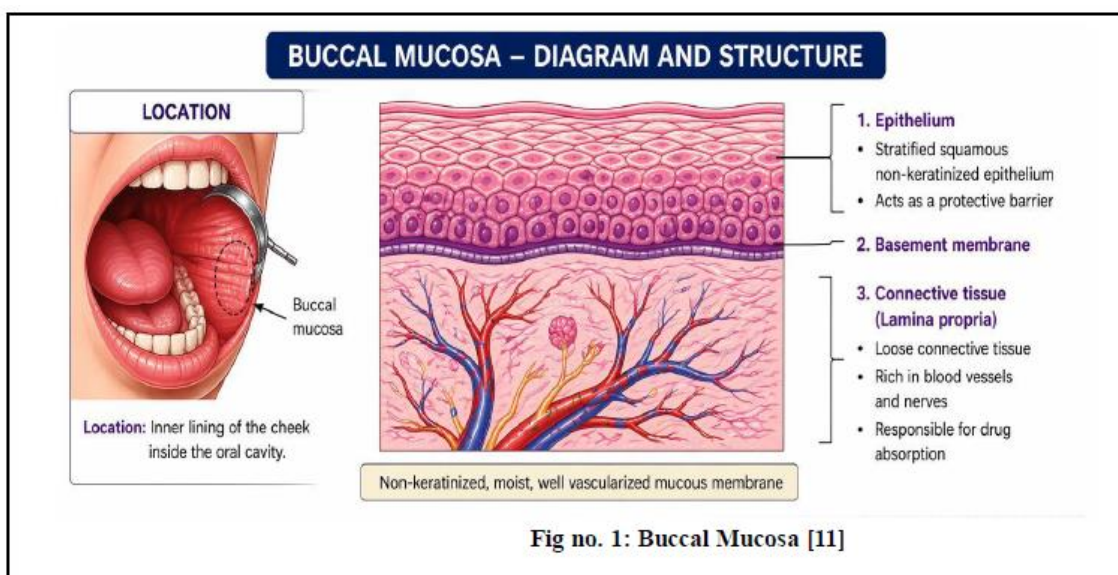
**BUCCAL MUCOSA<sup>[11]</sup>:** The buccal mucosa is a soft, moist, non-keratinized epithelial tissue present on the inner side of the cheeks. It is composed of multiple layers of cells and has a rich blood supply, which allows drugs to be absorbed directly into the systemic circulation. Because of this, it is widely used for drug delivery through buccal patches.

The structure of buccal mucosa mainly includes

- a) Epithelium (outer layer, acts as a barrier)

- b) Basement membrane
- c) Connective tissue (lamina propria)

One of the key features of buccal mucosa is its permeability, which is higher than skin but lower than sublingual mucosa. It is also less prone to irritation and has a relatively stable environment, making it suitable for controlled drug delivery.



### COMPOSITION OF BUCCAL PATCH<sup>[12]</sup>

Buccal patches are composed of various components such as the active pharmaceutical ingredient, mucoadhesive polymers, plasticizers, backing membrane, and permeation enhancers. Each component plays an important role in ensuring effective drug release, adhesion to the buccal mucosa, and improved therapeutic efficacy. The composition and selection of excipients significantly influence the performance of buccal patches.

**Advantages of Buccal Patches**<sup>[12]</sup>

1. Bypass first-pass metabolism
2. Improve bioavailability
3. Increase patient compliance
4. Reduce dosing frequency
5. Minimize side effects
6. Easy to use
7. Avoid GIT degradation

**How Buccal Patches Overcome the Limitations of Conventional Dosage Forms.**<sup>[13,14]</sup>

Sr. No	Limitation of Conventional Dosage Form	How Buccal Patches Overcome It
1.	First-pass metabolism in liver reduces drug bioavailability	Drug is absorbed directly through buccal mucosa → bypasses liver → increased Bioavailability
2.	Degradation in gastric environment (acid, enzymes)	Avoids stomach → protects drug from degradation
3.	Delayed onset of action (especially oral tablets)	Faster absorption through mucosa → quick onset
4.	Poor patient compliance (difficulty in swallowing tablets/capsules)	Easy to apply patch → improve compliance, especially in elderly and child
5.	Variable drug absorption due to food and GI condition	Buccal route gives more consistent absorption
6.	Systemic side effects due to high doses	Lower dose required → reduced side effects
7.	Drug instability in GI tract	Stable in buccal cavity → improves drug Stability
8.	Irritation of gastric mucosa (e.g., NSAIDs)	Avoids Gi tract → prevents gastric irritation
9.	Loss of drug due to vomiting or diarrhea	Buccal absorption unaffected → ensures proper dosing
10.	Lack of site-specific delivery	Can provide local action (e.g., periodontitis treatment)

**OBJECTIVES**<sup>[15,16,17]</sup>

- a) To bypass first-pass metabolism

Drugs are absorbed directly through the buccal mucosa, avoiding liver metabolism and improving drug efficiency.

- b) To improve patient compliance

Easy to administer, painless, and suitable for patients who have difficulty swallowing tablets.

- c) To achieve site-specific drug delivery

Useful for local treatment in the oral cavity (e.g., infections, ulcers, periodontitis).

d) To reduce dosing frequency

Sustained release reduces the need for frequent administration.

e) To minimize side effects

lower dose fluctuations help in reducing adverse effects.

f) The buccal patches of Metronidazole for the effective management of oral infections in diabetic patients.

g) To allow easy termination of therapy

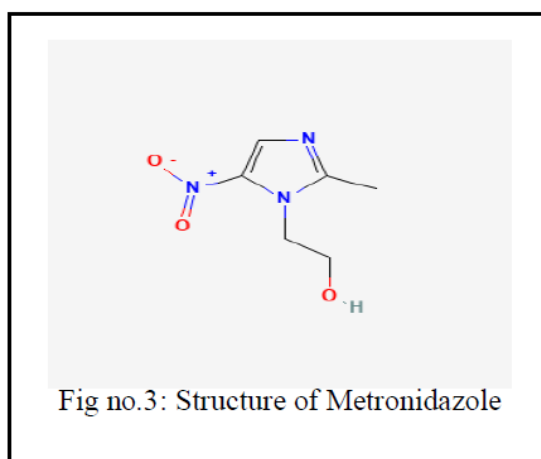
Patch can be removed easily in case of toxicity or irritation.

h) To improve drug stability

Protects drug from degradation in the gastrointestinal tract.

### DRUG PROFILE<sup>[18]</sup>

- Drug Name: Metronidazole
- Category: Nitroimidazole derivative
- Therapeutic Class: Antiprotozoal and antibacterial agent
- Chemical Name: 2-Methyl-5-nitroimidazole-1-ethanol
- Molecular Formula:  $C_6H_9N_3O_3$
- Molecular Weight: 171.15 g/mol
- Molecular Structure



➤ Mechanism of Action<sup>[19]</sup>: Metronidazole works by entering microbial cells and undergoing reduction of its nitro group. This produces toxic metabolites that.

- Disrupt DNA synthesis
- Cause DNA strand breakage

- Lead to cell death

It is mainly active against anaerobic bacteria and protozoa.

➤ Pharmacokinetics<sup>[19]</sup>

- Absorption: Well absorbed orally (bioavailability ~90–100%)
- Distribution: Widely distributed in body tissues, Crosses blood-brain barrier and placenta
- Metabolism: Metabolized in liver
- Half-life: ~6–8 hours
- Excretion: Mainly via urine

### PREFORMULATION STUDIES<sup>[19]</sup>

**Preformulation studies:** Preformulation studies are needed to ensure the development of a stable as well as therapeutically effective and safe dosage form. It is a stage of development during which characterizes the physio-chemical properties of the drug substances and its interaction with various formulation components.

#### Preformulation studies

1. **Physical Appearance<sup>[20]</sup>:** Metronidazole is a white to slightly yellow crystalline powder with a characteristic odour and bitter taste.
2. **Solubility<sup>[21]</sup>:** Metronidazole is soluble in ethanol and slightly soluble in water and phosphate buffer.
3. **Melting Point<sup>[22]</sup>:** The reported melting point of metronidazole is 159–163°C, indicating purity and stability of the drug.
4. **UV Spectroscopy<sup>[23,24]</sup>:** Metronidazole exhibits maximum absorbance around 277 nm and follows Beer-Lambert's law within a suitable concentration range.

### COMPOSITION OF BUCCAL PATCH<sup>[25]</sup>

SR.NO	COMPONENTS	ROLE	EXAMPLES
1	Active Pharmaceutical Ingredient	Provides therapeutic effect	Metronidazole
2	Polymers	Provide adhesion to be buccal and Control drug release rate	HPMC, HPC
3	Diluents	Increase bulk and improve handling	Micro Crystalline Cellulose, Starch
4	Sweeting Agent	Enhance patient compliance by improving taste	Sucralose, Mannitol
5	Flavouring agent	Mask unpleasant taste of drug	Menthol, Clove oil
6	Backing Layer	Provides unidirectional drug release	Ethyl Cellulose (EC)

		(towards mucosa) and prevents drug loss.	
7	Penetration Enhancer	Improve drug permeation through buccal mucosa.	Sodium lauryl sulfate (SLS)

## METHOD OF PREPARATION<sup>[26]</sup>

Various methods have been developed for the preparation of buccal patches depending on the nature of the drug, polymer characteristics, and desired release profile. The commonly used methods include solvent casting, direct milling, hot melt extrusion, semisolid casting, and solid dispersion techniques.

### 7.1 Solvent Casting Method

The solvent casting method is the most widely used technique for the preparation of buccal patches due to its simplicity, cost-effectiveness, and ability to produce uniform films. In this method, the required polymer is dissolved in a suitable solvent to form a homogeneous polymeric solution. The drug is dissolved separately and then mixed with the polymer solution along with plasticizers and other excipients. The resulting mixture is poured into a suitable mould or petri dish and allowed to dry under controlled conditions. After complete solvent evaporation, the dried film is removed and cut into patches of desired size.

### ADVANTAGES

- Simple and economical method
- Produces uniform films
- Suitable for heat-sensitive drugs
- Easy scale-up for industrial production
- Provides good drug distribution throughout the patch

For the formulation of Metronidazole buccal patches, the solvent casting method is considered highly suitable because Metronidazole is sensitive to high temperatures and requires uniform distribution within the polymer matrix.

### 7.2 Direct Milling Method

The direct milling method involves mixing the drug, polymer, and other excipients without the use of solvents. The resulting mixture is mechanically milled and compressed into thin films. This method eliminates the need for solvent removal and reduces processing time. However, achieving uniform drug distribution may be challenging.

### 7.3 Hot Melt Extrusion Method

Hot melt extrusion is a solvent-free technique in which the drug and polymer are mixed and heated above their softening point. The molten mass is then passed through an extruder to obtain thin films. This method is rapid and suitable for large-scale production. However, it may not be appropriate for thermolabile drugs.

### 7.4 Semisolid Casting Method

In the semisolid casting method, a viscous gel or semisolid mass containing drug and polymers is prepared. The semisolid mass is cast onto a suitable surface and dried to form thin films. This method is particularly useful for polymers that form highly viscous solutions.

### 7.5 Solid Dispersion Method

The solid dispersion method involves dispersing the drug uniformly within a carrier matrix before film formation. The prepared dispersion is then converted into a film by suitable techniques. This method improves drug solubility and dissolution characteristics, especially for poorly water-soluble drugs.

## EVALUATION PARAMETERS

1. **Weight Uniformity**<sup>[27]</sup>: Weight uniformity is determined to ensure that each buccal patch contains a uniform amount of formulation. Significant variations in weight may indicate non-uniform distribution of drug and excipients.

$$\text{Formula: Weight variation (\%)} = \frac{\text{Individual weight} - \text{average weight}}{\text{Average weight}} \times 100$$

2. **Thickness Uniformity**<sup>[27]</sup>: Thickness uniformity is evaluated using a micrometer screw gauge or vernier caliper at different points on the patch surface. Uniform thickness ensures reproducible drug release and adequate mechanical strength.
3. **Swelling Index**: Swelling index evaluates the ability of a buccal patch to absorb water and swell. It influences mucoadhesion and drug release behaviour of the formulation.
4. **Mucoadhesive Strength**: Mucoadhesive strength indicates the adhesive force between the buccal patch and mucosal surface. It ensures proper attachment of the patch and prolonged drug delivery at the site of application.
5. **Folding Endurance**<sup>[28]</sup>: Folding endurance represents the number of times a patch can be folded at the same place without breaking. It indicates flexibility and mechanical integrity

of the formulation.

6. **Surface Ph**<sup>[29,30]</sup>: Surface pH is measured to assess the compatibility of the buccal patch with the oral mucosa. The surface pH should be close to neutral to avoid irritation.
7. **Moisture Content**<sup>[31]</sup>: Moisture content determines the amount of water present in the formulation and plays an important role in stability and flexibility.

$$\text{Formula: Moisture Content (\%)} = \frac{W1-W2}{W2} \times 100$$

Where,

W1 = Initial weight W2= Final weight

8. **Moisture Absorption**<sup>[31]</sup>: Moisture absorption evaluates the hygroscopic nature of the formulation and its ability to absorb moisture from the surrounding environment.

$$\text{Formula: Moisture Absorption} = \frac{W2-W1}{W1} \times 100$$

Where,

W1= Initial weight W2= Final weight

9. **Drug Content Uniformity**<sup>[32,33]</sup>: Drug content uniformity ensures uniform distribution of the drug throughout the buccal patch and is essential for consistent therapeutic efficacy.
10. **In-vitro Drug Release Study**<sup>[34]</sup>: In-vitro drug release study is performed to determine the rate and extent of drug release from the buccal patch over time. It helps in evaluating the release pattern and therapeutic performance of the formulation.

## CONCLUSION

In conclusion, the formulated buccal patches of Metronidazole showed satisfactory physicochemical properties and were found to be suitable for buccal administration. The prepared formulations exhibited uniform drug content with acceptable evaluation parameters. The optimized formulation demonstrated the potential for effective buccal drug delivery with reduced dosing frequency and better patient compliance. The developed metronidazole buccal patches may also be beneficial for diabetic patients suffering from periodontal infections by providing localized drug delivery and improving therapeutic effectiveness. Therefore, metronidazole buccal patches can be considered a promising alternative to conventional dosage forms for the treatment of oral infections.

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