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# Overview On Buccal Patches: A Novel Approach for Enhanced Bioavailability and Compliance

***Mayur D. Shinde*, Amol U. Gayke, Vikas Shinde, Pradyumana Ige***
*SND College of Pharmacy Babhulgaon, Yeola, Nashik-423401*

****Corresponding Author***
*Email ID: shindemayur9209@gmail.com*

## ABSTRACT

*The buccal delivery of drugs through mucoadhesive patches has emerged as a promising alternative to conventional administration routes, particularly for drugs like Irbesartan, which exhibit poor oral bioavailability due to first-pass metabolism. This review explores the buccal patches for delivering Irbesartan, an angiotensin II receptor antagonist used in hypertension management. Irbesartan's poor solubility and high permeability (BCS Class II) make it an ideal candidate for buccal administration. Buccal patches provide several advantages, including improved bioavailability, controlled release, reduced dosing frequency, and enhanced patient compliance, while avoiding gastrointestinal degradation and hepatic metabolism. The formulation process involves selecting suitable mucoadhesive polymers and excipients to ensure effective drug release, adhesion, and permeation through the buccal mucosa. Various evaluation methods, such as physical characterization, drug release, and mucoadhesive strength, are critical to assessing patch performance. Additionally, the review highlights several marketed buccal patches that demonstrate the successful application of this technology for different therapeutic agents. In conclusion, Irbesartan buccal patches have the potential to enhance drug bioavailability, improve therapeutic efficacy, and offer a convenient alternative to oral administration, paving the way for future advancements in buccal drug delivery systems.*

***Keywords:*** *Irbesartan, buccal patch, bioavailability, Drug delivery, Hypertension, Formulation, Mucoadhesive.*

## INTRODUCTION

The administration of drugs through buccal patches has gained significant interest, particularly for drugs with low oral bioavailability like Irbesartan. Buccal drug delivery offers a non-invasive, easy-to-use alternative that bypasses first-pass metabolism, thus potentially improving drug absorption and patient compliance.[1-8] This review focuses on the formulation, evaluation, and potential benefits of buccal patches for delivering Irbesartan effectively. Irbesartan is an angiotensin II receptor antagonist used primarily to treat hypertension and nephropathy in diabetic patients.

It exhibits high selectivity for the AT1 receptor, which mediates its antihypertensive effect. However, Irbesartan suffers from poor oral bioavailability due to significant first-pass metabolism.[9] Irbesartan works by blocking the angiotensin II type 1 (AT1) receptors, thereby preventing vasoconstriction and aldosterone release.[10] This leads to relaxation of blood vessels, reduced blood pressure, and increased blood flow to the kidneys. Irbesartan is classified as a BCS Class II drug, indicating poor solubility but high permeability. This classification makes it an ideal candidate for buccal delivery to enhance bioavailability.[11]

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Buccal patches are adhesive dosage forms applied to the buccal mucosa. They offer advantages such as avoiding first-pass metabolism, improving patient compliance, and allowing controlled drug release. This method provides sustained drug release, reducing the frequency of dosing and minimizing side effects.[12-13]

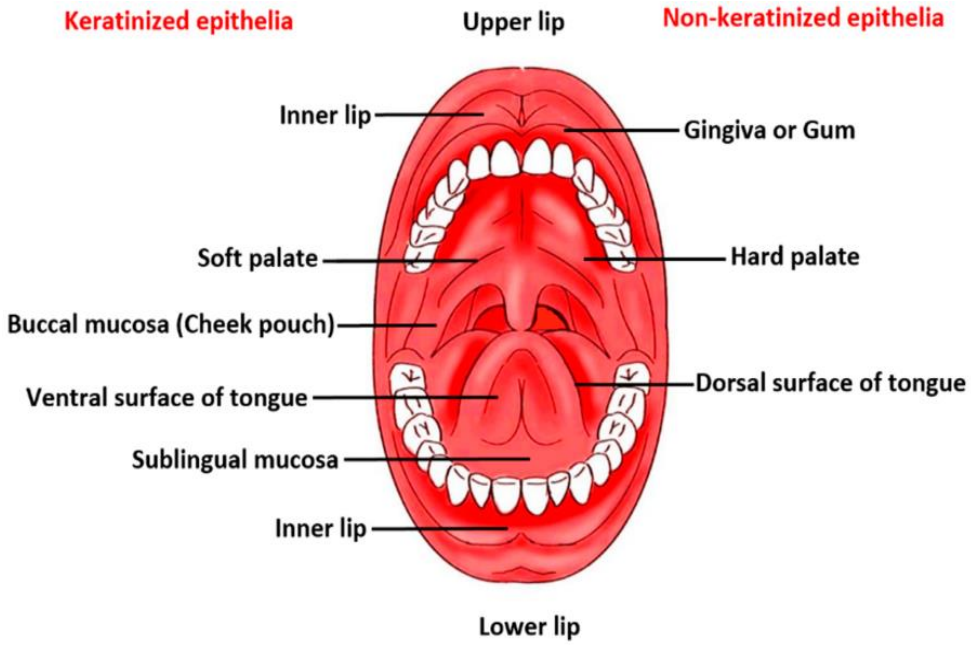


***Figure 1.*** *A schematic diagram depicting the key regions of the buccal area.*

## Why buccal patches better to other drug delivery system

### 1. Avoidance of First-Pass Metabolism

Drugs administered orally are typically metabolized in the liver before entering systemic circulation, which can significantly reduce bioavailability. Buccal patches, however, deliver drugs directly through the mucosal tissues in the mouth, bypassing the liver and avoiding this extensive first-pass metabolism. This improves the drug's bioavailability, especially for drugs that are metabolized extensively, like Irbesartan.[14]

### 2. Enhanced Bioavailability

By bypassing gastrointestinal (GI) degradation and liver metabolism, a larger proportion of the drug reaches systemic circulation. For drugs that are poorly absorbed or degraded in the stomach or intestines, buccal delivery is an effective way to achieve therapeutic levels with smaller doses.[15]

### 3. Controlled and Sustained Release

Buccal patches allow for controlled release of the drug over time. This steady release can maintain stable blood drug levels, reducing fluctuations that are common with other delivery methods, such as oral tablets, which have peak and trough concentrations. This stability can enhance therapeutic efficacy and reduce side effects.[16]

### 4. Improved Patient Compliance

Buccal patches are non-invasive, easy to use, and generally well-tolerated, which increases compliance, especially for patients who dislike or struggle with swallowing pills or receiving injections. The patch's discreet placement inside the mouth also makes it convenient for use throughout the day.[17]

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**5. Reduced Dosing Frequency**

Due to the sustained release profile, buccal patches can potentially reduce dosing frequency, which is particularly beneficial for drugs that require frequent administration. This further enhances patient compliance and simplifies treatment regimens.[18]

**6. Localized and Systemic Effects**

Buccal patches can be used for both localized treatment (e.g., treating oral infections or conditions) and systemic delivery (e.g., hypertension, as in the case of Irbesartan). This versatility makes them suitable for a wide range of therapeutic applications.[19]

**7. Minimized GI Side Effects**

Since buccal patches bypass the gastrointestinal tract, they avoid common GI side effects, such as nausea or irritation. This is advantageous for drugs that can cause gastric discomfort or for patients with conditions like irritable bowel syndrome or other GI sensitivities.[20]

**8. Rapid Onset of Action**

Buccal patches provide faster drug absorption into systemic circulation compared to some other routes (e.g., oral tablets), as the buccal mucosa is highly vascularized. This makes buccal patches ideal for medications that benefit from a faster onset, such as analgesics or anti-hypertensive agents.[21]

**9. Reduced Enzymatic Degradation**

Drugs delivered via the buccal route are less exposed to degrading enzymes found in the GI tract, which can degrade sensitive drugs before they reach the bloodstream.[22]

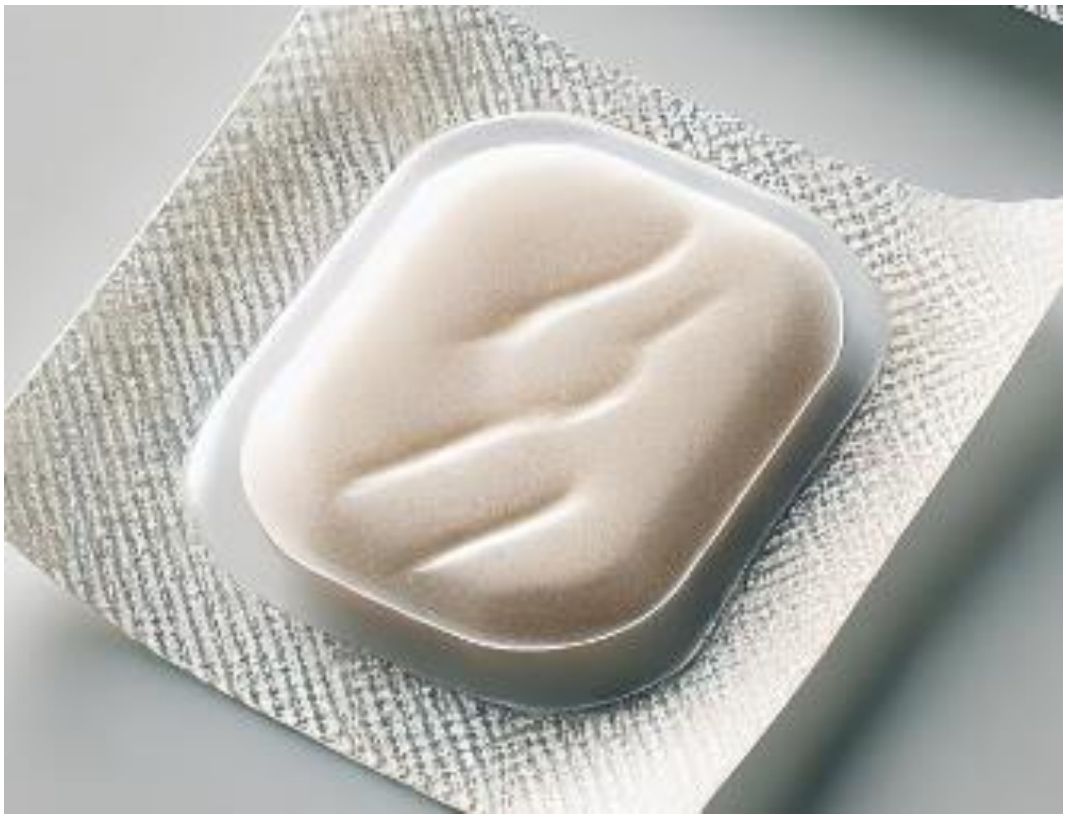

***Figure 2.*** *Marketed buccal patches.*

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**Table No 1. Formulation of Irbesartan Buccal Patches**

| Ingredient | Property |
|---|---|
| Irbesartan | Active drug |
| HPMC (Hydroxypropyl Methylcellulose) | Mucoadhesive polymer, controls drug release |
| Polyvinyl Alcohol (PVA) | Film-forming agent |
| Propylene Glycol | Plasticizer |
| Sodium Saccharin | Sweetening agent |
| Menthol | Flavoring agent |
| Ethanol | Solvent |

## MATERIALS AND METHODS

### a) Preparation of Buccal Patches:[23]

1. Dissolve Irbesartan in ethanol to prepare a uniform solution.
2. Mix mucoadhesive polymer and other excipients in the solution with continuous stirring.
3. Add plasticizer and flavoring agent, ensuring a homogeneous mixture.
4. Pour the mixture into a petri dish and allow it to dry at room temperature to form a thin film.
5. Cut the dried film into desired sizes for buccal patch application.

### b) Evaluation Tests[24]

1. **Physical Characterization:** Thickness, weight uniformity, folding endurance.
2. **Surface pH:** Ensures compatibility with buccal mucosa.
3. **Swelling Index**: Indicates hydration capability of the patch.
4. **Mucoadhesive Strength:** Measures the adhesive strength on the mucosal surface.
5. ***In Vitro* Drug Release Study**: Determines drug release rate over time.
6. **Permeation Studies**: Examines drug permeation through buccal tissue.

**Table 2. Examples of mucoadhesive buccal films based on their Therapeutic Category.[25-30]**

| Therapeutic Classification | Polymer/ Plasticizer | Active Ingredient | Manufacturing Method | Comments |
|---|---|---|---|---|
| Anti hypertensive | Chitosan, polyvinylpyrrolidone, PVA, gelatin/propylene glycol | Propranolol HCl | Solvent casting | Personalized bilayered buccal film useful for pediatric population |
| Antifungal | Dextran, maltodextrin, HPMC, HPC/PEG 400 and glycerol | Amphotericin B | Solvent casting | Mechanical strength of the film was contributed by Avicel 200 and Avicel CL611<br>Physically stable orodispersible film was effective in oropharyngeal candidiasis |
| Antiepileptic | HPMC | Diazepam | Solvent casting | Soluble film formulation of diazepam (Libervant™) effective in acute seizure emergencies<br>Dose can be adjusted by cutting the film of suitable size |
| Antiprotozoal /anti-inflammatory | HPMC, PVA, chitosan/glycerin | Ornidazole and dexamethasone sodium phosphate | Solvent casting | Double layered film demonstrated >95% drug release in 4 h<br>Significant effect on mucosal repair and reduced ulcer inflammation |

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| | | | | |
|---|---|---|---|---|
| Anesthetic/ analgesic and anti-inflammatory/ mucolytic | HPMC, NaCMC, Chitosan/propylene glycol and sorbitol | Lidocaine HCl, benzydamine HCl, N-acetyl-cysteine | Solvent casting | Biocompatible bilayered mucoadhesive film stimulates cell proliferation and demonstrated therapeutic effect in buccal mucositis |
| Anti-inflammatory | HPMC, ethyl cellulose, chitosan, NaCMC, carbopol 971P/propylene glycol, PEG 8000 | Fluticasone propionate | Solvent casting | Optimized formulation exhibited sustained drug release for 10 h Enhanced pharmacokinetic parameters was demonstrated compared to equivalent dose of mouthwash |

**Table 3: Marketed Buccal Patches**

| Brand Name | Active Ingredient | Indication | Description | Manufacturer |
|---|---|---|---|---|
| Belbuca | Buprenorphine | Chronic pain management | Adheres to the buccal mucosa for extended pain relief, bypassing first-pass metabolism. | Bio Delivery Sciences International |
| Onsolis | Fentanyl | Breakthrough cancer pain | Provides rapid pain relief by adhering to the cheek, allowing fentanyl absorption through mucosa. | Bio Delivery Sciences International |
| Striant | Testosterone | Hypogonadism in males | Sustained testosterone release through buccal mucosa for systemic absorption. | Columbia Laboratories, Inc. |
| Oravescent | Various drugs | Enhanced bioavailability | Uses effervescent technology for absorption of drugs like fentanyl and insulin via buccal mucosa. | Applied in multiple medications |
| Nitrogard | Nitroglycerin | Angina pectoris | Rapid nitroglycerin release through buccal mucosa to relieve chest pain. | Various generic manufacturers |
| Sitavig | Acyclovir | Herpes labialis (cold sores) | Localized acyclovir release for treating cold sores, adhering to the gum for direct action. | Bio Alliance Pharma SA |

## CONCLUSION

Irbesartan buccal patches present a promising formulation for overcoming low bioavailability associated with oral administration. This route provides sustained drug delivery, improved patient compliance, and reduced dosing frequency, making it an advantageous alternative to traditional formulations for antihypertensive therapy. Further research is warranted to optimize the formulation and evaluate its clinical efficacy.

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## REFERENCES

1) Gilhotra RM, Ikram M, Srivastava S, Gilhotra N. A clinical perspective on mucoadhesive buccal drug delivery systems. J Biomed Res. 2014 Mar;28(2):81-97.
2) Harris D, Robinson JR. Drug delivery via the mucous membranes of the oral cavity. J Pharm Sci. 1992;81:1–10.
3) Miller NS, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. Adv Drug Deliv Rev. 2005;57:1666–91. doi: 10.1016/j.addr.2005.07.003.
4) Puratchikody A, Prasanth VV, Mathew ST, Ashok KB. Buccal Drug Delivery: Past, Present and Future -A Review. Int. J. Drug Deliv. 2011;3:171–84.
5) Kianfar F, Antonijevic MD, Chowdhry BZ, Boateng JS. Formulation development of a carrageenan based delivery system for buccal drug delivery using ibuprofen as a model drug. J Biomater Nanobiotechnol. 2011;2:582–95.
6) Ahuja A, Khar RK, Ali J. Mucoadhesive Drug Delivery Systems. Drug Develop Indus Pharm. 1997;23:489–515.
7) Andrews GP, Laverty TP, Jones DS. Mucoadhesive Polymeric Platforms for Controlled Drug Delivery. Eur J Pharma Biopharm. 2009;71:505–18.
8) Woodley J. Bioadhesion: new possibilities for drug administration? Clin Pharmacokinet. 2001;40:77–84.
9) Croom KF, Curran MP, Goa KL, Perry CM. Irbesartan: a review of its use in hypertension and in the management of diabetic nephropathy. Drugs. 2004;64(9):999-1028.
10) Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I; Collaborative Study Group. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med. 2001 Sep 20;345(12):851-60.
11) Dudhipala N, Ettireddy S, Youssef AAA, Puchchakayala G. Cyclodextrin Complexed Lipid Nanoparticles of Irbesartan for Oral Applications: Design, Development, and In Vitro Characterization. Molecules. 2021 Dec 13;26(24):7538.
12) Fang Liu, Laxmi Kerai-Varsani, Tochukwu C. Okwuosa, Buccal films: A review of therapeutic opportunities, formulations & relevant evaluation approaches, Journal of Controlled Release, 2022;352:1071-1092.
13) Jacob S, Nair AB, Boddu SH, Gorain B, Sreeharsha N, Shah J. An updated overview of the emerging role of patch and film-based buccal delivery systems. Pharmaceutics. 2021 Aug 5;13(8):1206.
14) Kim J, De Jesus O. Medication Routes of Administration. [Updated 2023 Aug 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK568677/.
15) Gavhane YN, Yadav AV. Loss of orally administered drugs in GI tract. Saudi Pharm J. 2012 Oct;20(4):331-44.
16) Lodhi M, Dubey A, Narayan R, Prabhu P, Priya S. Formulation and evaluation of buccal film of Ivabradine hydrochloride for the treatment of stable angina pectoris. Int J Pharm Investig. 2013 Jan;3(1):47-53.
17) Shayeda Dharani S. Formulation and in vitro evaluation of mucoadhesive buccal patches of ondansetron hydrochloride. Int J Pharm Sci Nanotech. 2010;3:860–6.
18) Baryakova TH, Pogostin BH, Langer R, McHugh KJ. Overcoming barriers to patient adherence: the case for developing innovative drug delivery systems. Nat Rev Drug Discov. 2023 May;22(5):387-409.
19) Adhikari SN, Nayak BS, Nayak AK, Mohanty B. Formulation and evaluation of buccal patches for delivery of atenolol. AAPS PharmSciTech. 2010 Sep;11(3):1038-44.

20) Philpott HL, Nandurkar S, Lubel J, Gibson PR. Drug-induced gastrointestinal disorders. Frontline Gastroenterol. 2014 Jan;5(1):49-57.
21) Jacob S, Nair AB, Boddu SHS, Gorain B, Sreeharsha N, Shah J. An Updated Overview of the Emerging Role of Patch and Film-Based Buccal Delivery Systems. Pharmaceutics. 2021 Aug 5;13(8):1206.
22) Benet L. Intestinal MDR Transport proteins and P450 enzyme as barriers to oral drug delivery. J. Control Release. 1999;62:25–31.
23) Ikram M, Gilhotra N, Gilhotra RM. Formulation and optimization of mucoadhesive buccal patches of losartan potassium by using response surface methodology. Adv Biomed Res. 2015 Oct 29;4:239.
24) Lodhi M, Dubey A, Narayan R, Prabhu P, Priya S. Formulation and evaluation of buccal film of Ivabradine hydrochloride for the treatment of stable angina pectoris. Int J Pharm Investig. 2013 Jan;3(1):47-53.
25) Abruzzo, A.; Nicoletta, F.P.; Dalena, F.; Cerchiara, T.; Luppi, B.; Bigucci, F. Bilayered buccal films as child-appropriate dosage form for systemic administration of propranolol. *Int. J. Pharm.* 2017, *531*, 257–265.
26) Serrano, D.R.; Fernandez-Garcia, R.; Mele, M.; Healy, A.M.; Lalatsa, A. Designing fast-dissolving orodispersible films of amphotericin B for oropharyngeal candidiasis. *Pharmaceutics* 2019, *11*, 369.
27) Rogawski, M.A.; Heller, A.H. Diazepam buccal film for the treatment of acute seizures. *Epilepsy Behav.* 2019, *101*, 106537.
28) Zhang, C.; Liu, Y.; Li, W.; Gao, P.; Xiang, D.; Ren, X.; Liu, D. Mucoadhesive buccal film containing ornidazole and dexamethasone for oral ulcers: In vitro and in vivo studies. *Pharm. Dev. Technol.* 2019, *24*, 118–126.
29) Alves, T.F.R.; Rios, A.C.; da Silva Pontes, K.; Portella, D.L.; Aranha, N.; Severino, P.; Souto, E.B.; Gonsalves, J.K.M.; de Souza Nunes, R.; Chaud, M.V. Bilayer mucoadhesive buccal film for mucosal ulcers treatment: Development, characterization, and single study case. *Pharmaceutics* 2020, *12*, 657.
30) Ammar, H.O.; Ghorab, M.M.; Mahmoud, A.A.; Shahin, H.I. Design and in vitro/in vivo evaluation of ultra-thin mucoadhesive buccal film containing fluticasone propionate. *AAPS PharmSciTech* 2017, *18*, 93–103.