

Available online at [GSC Online Press Directory](https://www.gsconlinepress.com/)

GSC Biological and Pharmaceutical Sciences

e-ISSN: 2581-3250, CODEN (USA): GBPSC2

Journal homepage: <https://www.gsconlinepress.com/journals/gscbps>

(RESEARCH ARTICLE)



## A comprehensive review on buccal patches

Seema, Kapil kumar \* and Deepak Teotia

*Department of Pharmaceutics, Global Institute of Pharmaceutical Education & Research, Kashipur-244713, Uttarakhand, India.*

Publication history: Received on 25September 2020; revised on 05 October 2020; accepted on 10 October 2020

Article DOI: <https://doi.org/10.30574/gscbps.2020.13.1.0308>

### Abstract

Buccal Patches are the type of drug formulation that has normally a different course of administration through the buccal mucosa for drug delivery. The product is placed between upper gingiva (gums) and cheek to treat local and systemic conditions. Buccal patch have good accessibility to the membranes that line the oral cavity. These patches tend to help drug enter directly into the systemic circulation escaping hepatic first pass metabolism. This type of drug delivery method is considered useful for elevating the bioavailability of drugs. This review is a thorough study to apprehend the procedures involved in assessment of buccal patches and the modern approach towards this type of drug delivery. This article intends to analyze the overall profile of Buccal Patches and scope of future advances..

**KEYWORD:** Buccal mucosa; Buccal Patch/Film; Evaluation of buccal patches.

### 1. Introduction

Amongst the various routes of drug delivery, oral route is perhaps the most preferred to the patient and the clinician alike. However, per oral administration of drugs has disadvantages such as hepatic first pass metabolism and enzymatic degradation within the GI tract, that prohibit oral administration of certain classes of drugs especially peptides and proteins. Consequently, other absorptive mucous membrane are considered as potential sites for drug administration. Transmucosal routes of drug delivery (i.e., the mucosal linings of the nasal, rectal, vaginal, ocular and oral cavity) offer distinct advantages over oral administration for systemic drug delivery. These advantages include possible bypass of first pass effect, avoidance of presystemic elimination within the GI tract, and depending on the particular drug, a better enzymatic flora for the drug absorption<sup>1</sup>. Amongst the various routes of administration tried so far in the novel drug delivery systems, localized drug delivery to tissues of the oral cavity has been investigated for the treatment of periodontal disease (gum infection), bacterial and fungal infection. Over the decades mucoadhesion has become popular for its potential to optimize localized drug delivery by retaining a dosage form at the site of action (e.g. within the gastrointestinal tract) or systemic delivery by retaining the formulation in intimate contact with the absorption site (e.g. buccal cavity). Well defined bioadhesion is the ability of a material (synthetic or biological) to adhere to a biological tissue for an extended period of time<sup>2, 3, 4</sup>. The biological surface can be epithelial tissue or it can be the mucous membrane adhere on the surface of a tissue. If adhesion is to a mucous coat, the phenomenon is referred to as mucoadhesion. The use of mucoadhesive polymers in buccal drug delivery has a greater application<sup>3</sup>. Various mucoadhesive devices, including tablets, films, patches, disks, strips, ointments and gels have recently been developed. However, buccal patch offer greater flexibility and comfort than the other devices. In addition, a patch can circumvent the problem of the relatively short residence time of oral gels on mucosa, since the gels are easily washed away by saliva. Buccal route drug delivery provides the direct entry to the systemic circulation through the jugular vein bypassing the first pass hepatic metabolism leading to high bioavailability<sup>5, 6, 7</sup>. Other advantages such as excellent accessibility, low

\*Corresponding author: Seema Kapil kumar

Department of Pharmaceutics, Global Institute of Pharmaceutical Education & Research, Kashipur-244713, Uttarakhand, India.

enzymatic activity, suitability for drugs or excipients that mildly and reversibly damage or irritate the mucosa, painless administration, easy withdrawal, facility to include permeation enhancer/ enzyme inhibitor or pH modifier in the formulation, versatility in designing as multidirectional or unidirectional release system for local or systemic action<sup>8,9,10</sup>.

### 1.1. Advantages of buccal patches

- The oral mucosa has a rich blood supply. Drugs are absorbed from the oral cavity through the oral mucosa, and transported through the deep lingual or facial vein, internal jugular vein and in nominate vein into the systemic circulation.
- Buccal administration, the drug gains direct entry into the systemic circulation thereby bypassing the first pass effect. Contact with the digestive fluids of gastrointestinal tract is avoided which might be unsuitable for stability of many drugs like insulin or other proteins, peptides and steroids. In addition, the rate of drug absorption is not influenced by food or gastric emptying rate.
- The area of buccal membrane is sufficiently large to allow a delivery system to be placed at different occasions, additionally; there are two areas of buccal membranes per mouth, which would allow buccal drug delivery systems to be placed, alternatively on the left and right buccal membranes<sup>11</sup>.
- Buccal patch has been well known for its good accessibility to the membranes that line the oral cavity, which makes application painless and with comfort.
- Patients can control the period of administration or terminate delivery in case of emergencies<sup>12</sup>.
- The buccal drug delivery systems easily administered into the buccal cavity.
- The novel buccal dosage forms exhibit better patient compliance.

### 1.2. Limitations in buccal patches

- The area of absorptive membrane is relatively smaller. If the effective area for absorption is dictated by the dimensions of a delivery system, this area then becomes even smaller.
- Saliva is continuously secreted into the oral cavity diluting drugs at the site of absorption resulting in low drug concentrations at the surface of the absorbing membrane. Involuntary swallowing of saliva results in a major part of dissolved or suspended released drug being removed from the site of absorption. Furthermore, there is risk that the delivery system itself would be swallowed<sup>13</sup>.
- Drug characteristics may limit the use of the oral cavity as a site for drug delivery. Taste, irritancy, allergy and adverse properties such as discoloration or erosion of the teeth may limit the drug candidate list for this route. A conventional type of buccal drug delivery systems did not allow the patient concurrently eat, drink or in some cases, talk<sup>14</sup>.

---

## 2. Method of Preparation

### 2.1. Solvent casting

In this method, all patch excipients including the drug co-dispersed in an organic solvent and coated onto a sheet of release liner. After solvent evaporation a thin layer of the protective backing material is laminated onto the sheet of coated release liner to form a laminate that is die-cut to form patches of the desired size and geometry<sup>15</sup>.

### 2.2. Direct milling

In this, patches are manufactured without the use of solvents. Drug and excipients are mechanically mixed by direct milling or by kneading, usually without the presence of any liquids. After the mixing process, the resultant material is rolled on a release liner until the desired thickness is achieved. The backing material is then laminated as previously described. While there are only minor or even no differences in patch performance between patches fabricated by the two processes, the solvent-free process is preferred because there is no possibility of residual solvents and no associated solvent-related health issues<sup>16</sup>.

#### 2.2.1. Evaluations of buccal patch

##### Surface pH

Buccal patches are left to swell for 2 hr on the surface of an agar plate. The surface pH is measured by means of a pH paper placed on the surface of the swollen patch<sup>11</sup>.

### Thickness measurements

The thickness of each film is measured at five different locations (centre and four corners) using an electronic digital micrometre<sup>17</sup>.

### 2.3. Swelling study

Buccal patches are weighed individually (designated as W1), and placed separately in 2% agar gel plates, incubated at 37°C ± 1°C, and examined for any physical changes. At regular 1hour time intervals until 3 hours, patches are removed from the gel plates and excess surface water is removed carefully using the filter paper<sup>18,19</sup>.

The swollen patches are then reweighed (W2) and the swelling index (SI) is calculated using the following formula.

$$SI = (W2 - W1) \times 100$$

W1

### 2.4. Folding endurance

The folding endurance of patches is determined by repeatedly folding 1 patch at the same place until it breaks or is folded up to 200 times without breaking<sup>20</sup>.

#### 2.4.1. Water absorption capacity test

Circular Patches, with a surface area of 2.3 cm<sup>2</sup> are allowed to swell on the surface of agar plates prepared in simulated saliva (2.38 g Na<sub>2</sub>HPO<sub>4</sub>, 0.19 gKH<sub>2</sub>PO<sub>4</sub>, and 8 g NaCl per liter of distilled water adjusted with phosphoric acid to pH 6.7), and kept in an incubator maintained at 37°C ± 0.5°C. At various time intervals (0.25, 0.5, 1, 2, 3, and 4 hours), samples are weighed (wet weight) and then left to dry for 7 days in a desiccators over anhydrous calcium chloride at room temperature then the final constant weights are recorded. Water uptake (%) is calculated using the following equation<sup>21</sup>.

$$\text{Water uptake(\%)} = (WW - Wf) \times 100$$

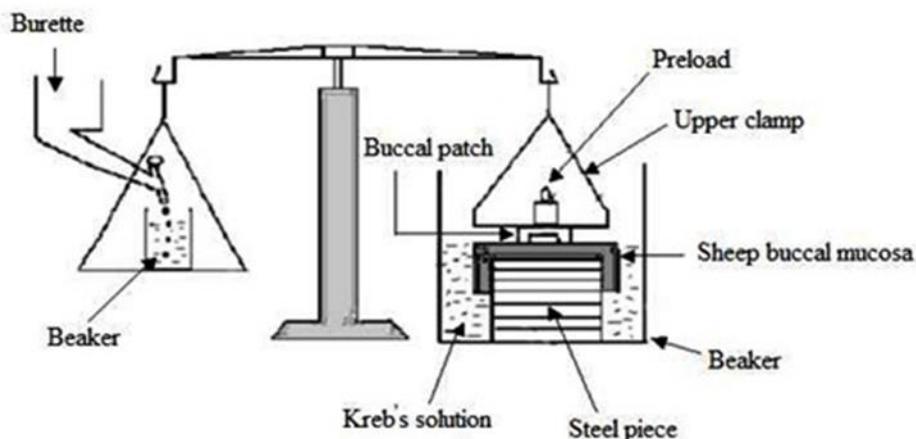
Wf

Where,

Ww is the wet weight and Wf is the final weight. The swelling of each film is measured<sup>22,23</sup>.

### 2.5. Ex-vivo bio adhesion test

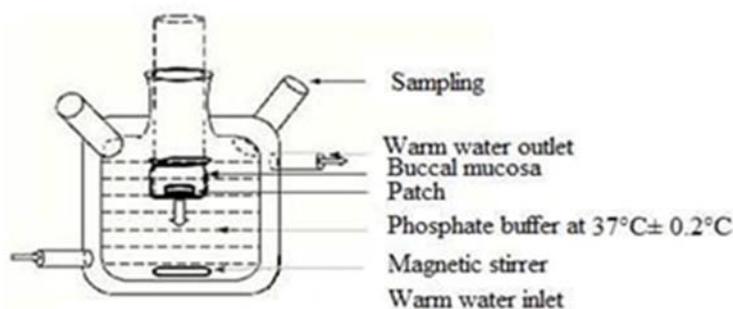
The fresh sheep mouth separated and washed with phosphate buffer (pH 6.8). A piece of gingival mucosa is tied in the open mouth of a glass vial, filled with phosphate buffer (pH 6.8). This glass vial is tightly fitted into a glass beaker filled with phosphate buffer (pH 6.8, 37°C ± 1°C) so it just touched the mucosal surface. The patch is stuck to the lower side of a rubber stopper with cyano acrylate adhesive. Two pans of the balance are balanced with a 5-g weight. The 5-g weight is removed from the left hand side pan, which loaded the pan attached with the patch over the mucosa. The balance is kept in this position for 5 minutes of contact time. The water is added slowly at 100 drops/min to the right-hand side pan until the patch detached from the mucosal surface.<sup>[18]</sup> The weight, in grams, required to detach the patch from the mucosal surface provided the measure of mucoadhesive strength<sup>24,25</sup>. (Figure 1).



**Figure 1** Measurement of mucoadhesive strength

## 2.6. *In vitro* drug release

The United States Pharmacopoeia (USP) XXIII-B rotating paddle method is used to study the drug release from the bilayered and multi-layered patches. The dissolution medium consisted of phosphate buffer pH 6.8. The release is performed at  $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ , with a rotation speed of 50 rpm. The backing layer of buccal patch is attached to the glass disk with instant adhesive material. The disk is allocated to the bottom of the dissolution vessel. Samples (5 ml) are withdrawn at predetermined time intervals and replaced with fresh medium. The samples filtered through Whatman filter paper and analysed for drug content after appropriate dilution. The *in-vitro* buccal permeation through the buccal mucosa (sheep and rabbit) is performed using Keshary-Chien/Franz type glass diffusion cell at  $37^{\circ}\text{C} \pm 0.2^{\circ}\text{C}$ . Fresh buccal mucosa is mounted between the donor and receptor compartments. The buccal patch is placed with the core facing the mucosa and the compartments clamped together. The donor compartment is filled with buffer 26-28 (Figure 2).



**Figure 2** Schematic diagram of Franz diffusion cell for buccal patch

## 2.7. Permeation study of buccal patch

The receptor compartment is filled with phosphate buffer pH 6.8, and the hydrodynamics in the receptor compartment is maintained by stirring with a magnetic bead at 50 rpm. Samples are withdrawn at predetermined time intervals and analysed for drug content<sup>29</sup>.

## 2.8. *Ex-vivo* mucoadhesion time

The *ex-vivo* mucoadhesion time performed after application of the buccal patch on freshly cut buccal mucosa (sheep and rabbit). The fresh buccal mucosa is tied on the glass slide, and a mucoadhesive patch is wetted with 1 drop of phosphate buffer pH 6.8 and pasted to the buccal mucosa by applying a light force with a fingertip for 30 seconds. The glass slide is then put in the beaker, which is filled with 200 ml of the phosphate buffer pH 6.8, is kept at  $37^{\circ}\text{C} \pm 1^{\circ}\text{C}$ . After 2 minutes, a 50-rpm stirring rate is applied to simulate the buccal cavity environment, and patch adhesion is monitored for 12 hours. The time for changes in colour, shape, collapsing of the patch, and drug content is noted<sup>30,31</sup>.

## 2.9. Stability study in human saliva

The stability study of optimized bi-layered and multi-layered patches is performed in human saliva. The human saliva is collected from humans (age 18-50years). Buccal patches are placed in separate Petri dishes containing 5ml of human saliva and placed in a temperature-controlled oven at  $37^{\circ}\text{C} \pm 0.2^{\circ}\text{C}$  for 6 hours. At regular time intervals (0, 1, 2, 3, and 6 hours), the dose formulations with better bioavailability are needed. Improved methods of drug release through transmucosal and transdermal methods would be of great significance, as by such routes, the pain factor associated with parenteral routes of drug administration can be eliminated. Buccal adhesive systems offer innumerable advantages in terms of accessibility, administration and withdrawal, retentively, low enzymatic activity, economy and high patient compliance. Adhesion of buccal adhesive drug delivery devices to mucosal membranes leads to an increased drug concentration gradient at the absorption site and therefore improved bioavailability of systemically delivered drugs. In addition, buccal adhesive dosage forms have been used to target local disorders at the mucosal surface (e.g., mouth ulcers) to reduce the overall dose required and minimize side effects that may be due to systemic administration of drugs. Researchers are now looking beyond traditional polymer networks to find other innovative drug transport systems. Currently solid dosage forms, liquids and gels applied to oral cavity are commercially successful. The future direction of buccal adhesive drug delivery lies in vaccine formulations and delivery of small proteins/peptides<sup>15,16</sup>.

---

## 3. Conclusion

The buccal mucosa offers several advantages for controlled drug delivery for extended periods of time. The mucosa is well supplied with both vascular and lymphatic drainage and first-pass metabolism in the liver and pre-systemic elimination in the gastrointestinal tract are avoided. The area is well suited for a retentive device and appears to be acceptable to the patient. With the right dosage form design and formulation, the permeability and the local environment of the mucosa can be controlled and manipulated in order to accommodate drug permeation. Buccal drug delivery is a promising area for continued research with the aim of systemic delivery of orally inefficient drugs as well as a feasible and attractive alternative for non-invasive delivery of potent peptide and protein drug molecules. However, the need for safe and effective buccal permeation/absorption enhancers is a crucial component for a prospective future in the area of buccal drug delivery.

---

## Compliance with ethical standards

### *Acknowledgments*

Authors are thankful for Dr. A.K. Saxena for his motivation and suggestion during the literature survey.

### *Disclosure of conflict of interest*

No conflict of interest is associated with this work.

---

## References

- [1] Shidhaye SS, et al. Mucoadhesive bilayered patches for administration of sumatriptan. *AAPS pharm sci tech.* 2009; 9(3): 1-13.
- [2] Giradkar KP, et al. Design development and in vitro evaluation of bioadhesive dosage form for buccal route. *International journal of pharma research & development.* 2010; 2: 1-24.
- [3] Amir H, et al. Systemic drug delivery via the buccal mucosal route, *Pharmaceutical technology.* 2001; 1-27.
- [4] Fatima AA, Chukwuka UK. Development and *in-vitro* evaluation of matrix-type transdermal patches of losartan potassium. *Universal Journal of Pharmaceutical Research.* 2017; 2(2): 16-20.
- [5] Steward A, et al. The Effect of Enhancers on the Buccal Absorption of Hybrid (BDBB) Alpha-Interferon. *IntJ Pharm.* 1994; 104: 145–149.
- [6] Al-kaf AGA, Othman AM. Pharmacosomes: an Updated review, *Universal Journal of Pharmaceutical Research.* 2017; 2(1): 30-33.
- [7] Mishra S. A Review article: Recent Approaches in buccal patches, the pharma innovation. 2012;7(2):78-86.
- [8] AJ Hoogstraate, et al. Diffusion Rates and Transport Pathways of FITC-Labelled Model Compounds through Buccal Epithelium, *Proc. Int. Symp. Contr. Rel. Bioact. Mater.* 1993;20:234–235.

- [9] Bhartee P, Kapil Kumar. Buccal drug delivery system: a tool for the effective delivery of pharmaceuticals. *Universal Journal of Pharmaceutical Research*. 2017; 2(3): 19-24.
- [10] Ryan FD, Paul AM, Agnieszka AZ, David W. Design and physicochemical characterization of a bioadhesive patch for dose controlled topical delivery of imiquimod. *Int J Pharm*. 2006;307:3 18-25.
- [11] Shafiullah D, Pramodkumar TM, Shivakumar HG. Formulation and evaluation of chlorhexidine mucoadhesive drug delivery systems. *Ind Drugs*. 2006;43(2): 122-5.
- [12] Diojad RC, Manvi FV, Malleshwarrao VSN, Patel PS. Buccoadhesive drug delivery system of isosorbide dinitrate: Formulation and evaluation. *Ind J Pharm Sci*. 2006;68(6):744-8.
- [13] Thimmasetty J, Subramanyam CVS, Manish kumar DS, Manjunath K, Shivanand K. Design and evaluation of fexofenadine HCl buccal mucoadhesive patches. *Biomed*. 2007; 2(1):73-83.
- [14] Güneşm Karavana SY, Algin Yapar E. Buccal drug delivery system: an overview about dosage forms and recent studies. *Universal Journal of Pharmaceutical Research*. 2019; 4(6):69-74.
- [15] Mona S, Semalty A, Kumar G. Formulation and characterization of mucoadhesive buccal patches of glipizide. *Ind J Pharm Sci*. 2008; 70(1):43-8.
- [16] Goudanavar PS, et al. Formulation and *In-vitro* evaluation of mucoadhesive buccal films of Glibenclamide, *Der pharmacialettere*. 2010; 2 (1): 382-387.
- [17] Okoro-chukwu Nnamdi, Ihuaku Emmanuel C. Development and characterization of mucoadhesive patches for buccal delivery of pregabalin. *Universal Journal of Pharmaceutical Research*. 2017; 2(3): 6-9.
- [18] Choudhary A, et al. Formulation and characterization of carvedilol buccal mucoadhesive patches, [www.ijrps.pharmascope.org](http://www.ijrps.pharmascope.org). 2010; 1(4): 396-401.
- [19] Kamel AH, et al. Micromatrical metronidazole benzoate film as a local mucoadhesive delivery system for treatment of periodontal diseases, *AAPS pharmscitech*. 2007; 8(3): 75.
- [20] Francis DJE. Development and evaluation of matrix type transdermal patches of pioglitazone hydrochloride. *Universal Journal of Pharmaceutical Research*. 2016; 1(1): 17-20.
- [21] Igwe J. Chibueze, Emenike IV, Oduola AR. Formulation and evaluation of Finasteride sustained-release matrix tablets using different rate controlling polymers. *Universal Journal of Pharmaceutical Research*. 2016; 1(2): 15-18
- [22] Giradkar KP, et al. Design development and *in vitro* evaluation of bioadhesive dosage form for buccal route, *International journal of pharma research & development*. 2010; 2.
- [23] Agarwal P, Semimul AA. comprehensive review on sustained release matrix tablets: a promising dosage form. *Universal Journal of Pharmaceutical Research*. 2018; 3(6): 49-54.
- [24] Leung SS, JR Robinson, Polymer Structure Features Contributing to Mucoadhesion II, *J. Contr.Rel*. 1990; 12: 187–194.
- [25] Gandhi RE, Robinson JR, Bioadhesion in Drug Delivery, *Indian J. Pharm. Sci.* (May/June) 1988; 50: 145–152.
- [26] Peter OI, Ifeoma UC. Development and evaluation of Albendazole microcapsule for colonic drug delivery system. *Universal Journal of Pharmaceutical Research*. 2017; 2(2): 4-7.
- [27] Maad AH, Shayoub MEA, Elnima EI, Osman Z, Magbool FF. Formulation and evaluation of colon targeted matrix tablets containing extract of *Solenostemma Argel* (Hargel). *Universal Journal of Pharmaceutical Research*. 2019; 4(4): 33-38.
- [28] Sanzgiri YD, et al. Evaluation of Mucoadhesive Properties of Hyaluronic Acid Benzyl Esters, *Int. J.Pharm*. 1994; 107: 91–97.
- [29] Kumar A, Kumar K. Solid dispersion-strategy to enhance solubility and dissolution of poorly water soluble drugs. *Universal Journal of Pharmaceutical Research*. 2017; 2(5): 50-55.
- [30] Park K, Robinson JR, Bioadhesive Polymers as Platforms for Oral Controlled Drug Delivery, Method to Study Bioadhesion, *Int. J. Pharm*. 1984; 19: 107–127.
- Sunday OS. Colon-targeted drug delivery systems: design, trends and approaches. *Universal Journal of Pharmaceutical Research*. 2017; 2(4): 46-50.