EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 11
Issue: 2
148-153
Year: 2024

A REVIEW ON BUCCAL DRUG DELIVERY SYSTEM

Punam Narwade*, Pallavi Mhaske, Aijaz Sheikh and K. R. Biyani

Department of Pharmaceutics, Anuradha College of Pharmacy, Chikhli, Buldhana-443201.

***Corresponding Author: Punam Narwade**
Department of Pharmaceutics, Anuradha College of Pharmacy, Chikhli, Buldhana-443201.

Article Received on 10/12/2023 **Article Revised on 30/12/2023** **Article Accepted on 20/01/2024**

ABSTRACT
Oral drug delivery is a promising traditional method that involves placing drugs inthe mouth for direct absorption through the mucosa. This method bypasses first- pass metabolism, increasing the bioavailability of the drug, allowing the child to take more of it. Controlled-release and release enhanced procedures help improve treatment outcomes and have no impact on pati ent compliance. However, challenges such as masking, absorption differences, andmucosal irritation require careful design. Despite these problems, research is const antly seeking to improve the oral cavity, make it usable, and update the drug delive ry strategy, balancing efficiency and patient acceptance.

KEYWORDS: Oral drug delivery, polymers, oral mucosa, saliva, oral route, first pass metabolism,intracellular.

INTRODUCTION

Oral administration is one of the alternatives to oral administration, especially in firs tline drugs.[1] Stratified squamous epithelium, supported by the lamina propria of c onnective tissue found in the buccal mucosa[2], was proposed as a site of drug deli very many years ago. Problems related to the oral administration route, such as high metabolism in the liver, poor absorption of the drug in the gastrointestinal tract in se vere cases, and the effect of parenteral administration, can be solved by oral administ ration.[3, 4]

The oral method seems to have many advantages, such as good access, physical han dling, use of information as needed, and less sensitivity to the task. For this reason, mucosal dosage forms are prepared as oral adhesive tablets[5,6], adhesive sticks[7,8] and adhesive sticks.[9]

Membrane penetration of hydrophilic substances is one of the major limitations in th e production of oral bioadhesive materials. Buccal mucosal epithelium is the main b arrier of drug absorption.[10] Various methods have been proposed to increase oral absorption. By changing the physical and chemical strength of the drug, the permeab ility of the drug through the buccal membrane can be increased and the degradation of the drug by enzymes can be prevented.[11] Additionally, enhanced bioadhesion an d release properties of oral agents may increase drug absorption.[12]

Incorporating absorption enhancers into oral formulations is an interesting approach.Drugs that promote penetration through the oral mucosa are called penetration enha ncers.[13]

Different mechanisms of effective penetration have been studied for oral use to increase drug penetration.[14,15]

The complexation of steroidal hormones with cyclodextrins was not effective in incr easing the permeation through buccal route, whereas condensation products of cyclo dextrin with propylene oxide or epi chlorohydrins were able to form complexes withestradiol, testosterone, and progesterone, thereby enhancing absorption through thebuccal membrane in humans.[16]

The delivery of hydrophilic macromolecular drugs via buccal membrane was made p ossible by incorporation of absorption or permeation enhancers, which could reduce barrier pro perties of the buccal epithelium.[17] The aim of the present study was to discuss abo ut oral mucosa and approaches for buccal drug delivery system.

Ideal Characteristics of Buccal Drug Delivery

An ideal BDDS should have following characteristics

- Polymer and its decaying derivatives should be harmless and free from leaching toxins.
- Should have good adhesive properties and mechanical strength. Bio-adhesive set should be ductile and have firmness.
- Polymer should be readily accessible and cost-effective.
- Should demonstrate both dry and liquid bio-adhesive properties.

- If inhibition and penetration properties in local enzymes are shown, they should have.
- adhesively active groups. Molecular weights should be optimal.
- Must indicate acceptable shelf-life.
- Spatial confirmation is necessary.
- Should have good bonding nature.
- Should stick for few hours to the attachment site.
- Subject to controlled release of the medication.
- Should have unidirectional drug release into the mucosa.
- Should effectively enhance absorption rate and duration of medication.
- Should not irritate patient or trigger any discomfort.
- Should not affect basic processes such as speaking and drinking.[18,19]

Advantages Buccal Drug Delivery

- Bypass the first-pass effect and nonexposure of the drugs to the gastrointestinal fluids.[20]
- Easy access to membrane areas for easy application, insertion and removal of the dispersion.[20]
- It increases the activity of many drugs due to longer contact times with the mucosa.[20]
- Higher patient acceptance compared to other non-oral application methods.[20]
- Tolerates sensitivities (compared to nose and skin).[20]
- Spending more time with controlled API release may reduce the frequency of druguse.[20]
- Due to the location of the API, a significant reduction in cost and a reduction in side effects resulting from drug use can also be achieved. source of the disease.[21]
- Due to adhesion and affinity, the formulation remains at the site of delivery longer, thus increasing API bioavailability using lower API concentrations to treat disease.[21]
- The harsh environment of oral drug delivery can be avoided by oral drug delivery.[22]

Disadvantages Oral Administration

Oral administration is not suitable for large doses (please specify size or quantity).

- small area, small absorption area.
- In this way, good nutrition is associated with drug delivery. Drugs with a risk of ora l pH imbalance should not be prescribed in this way.[23,24,25]

Structure of the Oral Mucosa

The oral mucosa has an outer layer consisting of multilayered epithelium. Below th is is the basement membrane, lamina propria and the inner layer is the submucosa.

The epithelium is similar to the stratified squamous epithelium found elsewhere in the body. Cells are released from the epithelial surface as it has a mitotically active basal cell layer that rises to the surface through various intermediate layers. The th ickness of the buccal mucosal epithelium is approximately 40_50 times, while the thickness of the sublingual epithelium is slightly less. Epithelial cells grow larger an d better as they progress from the basal to the outer layers. The renewal period of the buccal epithelium is approximately 56 days, and this period can represent the en tire oral mucosa. The thickness of the oral mucosa varies depending on location: the thickness of the buccal mucosa is 500_800 µm, and the thickness of the mucosa on the palate, soft palate, floor of the mouth, tongue and gums is approximately 100 µm -200. do it.

The function of saliva

1. It is the protective fluid for all tissues in the mouth.
2. The enamel continues to mineralize.
3. The oral mucosa is too moist.

Functions of mucus

1. It contains high amounts of protein and carbohydrates.
2. Cell-cell adhesion.
3. lubrication.
4. Bioadhesion of the mucoadhesive drug carrier system.

Permeability

The oral mucosa is generally a slightly leaky epithelium between the epidermis and the intestinal mucosa. It is estimated that the oral mucosa is 4-4000 times more permeable than the skin. Generally speaking, the order of decreas e in the permeability of the oral mucosa is sublingual rather than buccal, buccal rat her than palatal. This ranking is based on the relative thickness of the tissues and th e degree of keratinization; the sublingual mucosa is relatively thin and non-keratinized, the buccal mucosa is thick and non-keratinized, and the palate is slightly thicker but keratinized.[11,26]

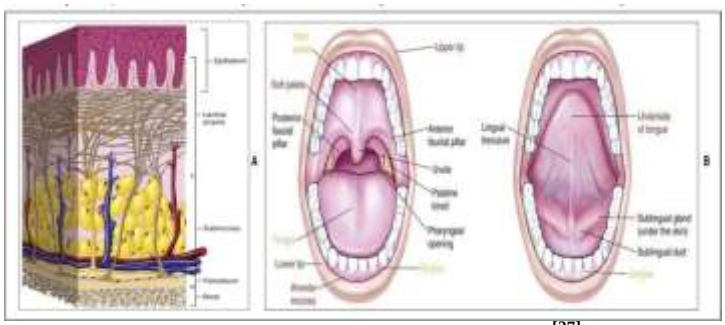

Figure 1: Anatomy of Oral Mucosa.[27]

New Buccal Mucosal Dosage Forms

New Buccal Mucosal Dosage Forms include buccal mucosal tablets, patches, films, semisolids (ointments and gels), and powders.[28]

- **Buccal Mucosal Tablets**

These are prepared dry. must be moistened before reaching the buccal mucosa. Fo r example, a two-layer tablet whose adhesive matrix is the hydroxypropylcellulose layer and the center is cocoa butter contains insulin andsodium glycocholate.[29]

- **Patches and Films**

The chin patch consists of two laminate layers with aqueous adhesive polymer plac ed on an impermeable backsheath structure provided by the model divided into elli ptical patterns. Zilactin is a special mucoadhesive membrane produced by dissolving organic acids, alcohol and hydroxypropylcellulose. When applied to the oral mucosa, the film remains in place for up to 12 hours.[29] The oral matrix is a gel- based oral formulation that remains in place for 15-150 minutes.[29]

- **Powder**

The powder form of HPC and beclomethasone sprayed into the BM of rats was fou nd to be better in terms of time compared to 2.5% beclomethasone for oral solution and long-term BM. More than four hours.[29]

Types and forms of buccal dosage forms

The two types of buccal dosage forms are matrix and depot

A. Matrix type: Patch formula contains chemicals, adhesives and mixed ingredients.

B. Reservoir Type: The structure of the buccal patch has a different chemical cham ber and adhesive in the reservoir system. Use an impermeable support to prevent dr ug degradation, prevent deformation and cracking in the mouth, and monitor drug distribution.[30]

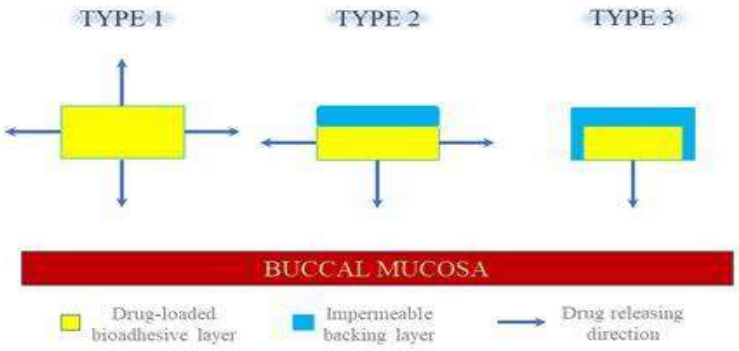

Figure 2: Kinds of buccal mucoadhesive dosage form.[31]

Buccal Absorption Mechanism

There are two mechanisms for drug absorption through the squamous stratified epithelium of the oral mucosa

i. Transcellular (in one cell, from one cell).
ii. Paracellular (between cells, bypassing cells).

It has been reported that penetration into the buccal mucosa is a process m ainly through the synthesis of lipids produced by the membrane.[26]

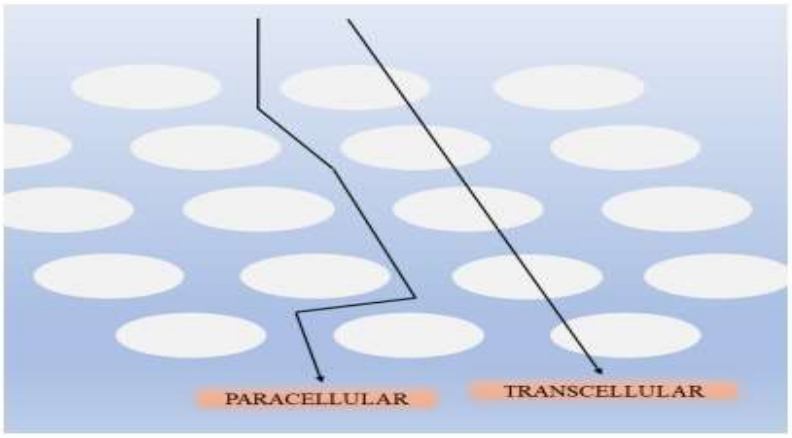

Figure 2: Diagrammatic representation of pathways for drug delivery via oralcavity mucosa.[31]

FACTORS AFFECTING BUCCAL ABSORPTION

Table 1: Various permeation enhancers utilized in buccal drug delivery.[32] Membrane factors.

Class of permeation enhancers	Example
Bile salts	Sodium deoxycholate, sodium glycocholate, sodium glycodeoxycholate, sodium taurocholate, sodiumtaurodeoxycholate.
Chelators	Citric acid, EDTA, methoxy salicylates, sodium salicylate
Fatty acids	Capric acid, lauric acid, lysophosphatidylcholine, methyloleate, Oleic acid, phosphatidylcholine.
Inclusion complexes	Cyclodextrins
Non-surfactants	Unsaturated cyclic ureas.
Surfactants	Polyoxyethylene, sodium lauryl sulphate
Others	Sulfoxides, polysorbate 80, dextran sulfate, cyclodextrin, azone

Degree of keratinization, surface area available for absorption, mucus layer of the sal ivary membrane, intercellular lipids of the epithelium, basement membrane and lamina propria. Additionally, absorbent film thickness, blood supply/lymphatic fluid, cell renewal and enzyme content will help reduce the amount and cost of drugs enteringthe body.

2. Environmental Factors

A. Saliva

A thin film of saliva covers the entire mucosa and is called salivary film or membrane e. The thickness of the saliva film is 0.07 to 0.10 mm. The thickness, composition, and movement of these films affect oral absorption.

B. Salivary glands

Minor salivary glands are located in the epithelial or deep epithelial region of the buc cal mucosa. They constantly secrete mucus on the surface of the oral mucosa. Although mucus helps retain mucoadhesive drugs, it also hinders drug penetration.

C. Movement of tissue

There is less movement in the buccal area of the mouth. Mucoadhesive polymers may be added to maintain the oral dose for extended periods of time to prevent tissue m ovement during speaking and possibly eating or swallowing.[33]

Formulation Related Factors

1. Membrane Factors

These include the degree of keratinization, resorbable area, mucus layer of the saliva ry membrane, epithelial lipids, basement membrane and lamina propria. Additionall y, absorbent film thickness, blood supply/lymphatic fluid, cell renewal and enzyme c ontent will help reduce the amount and cost of drugs entering the body.

2. Environmental factors

A. Saliva

Saliva film covers the entire buccal mucosa, called salivary film or membrane. The thickness of the saliva film is 0.07 to 0.10 mm. The thickness, composition and movement of this membrane affect the rate of buccal absorption.

B. Salivary glands

Minor salivary glands are located in the epithelial or deep epithelial region of the buc cal mucosa. They constantly secrete mucus on the surface of the oral mucosa. Although mucus helps retain mucoadhesive drugs, it also hinders drug penetration.

C. Movement of tissues

Weakness is seen in the mouth area. The mucoadhesive pol ymers are to be incorporated to keep dosage form at buccal region for long periods to withstand tissue movements during talking and if possible during eating food or swa llowing.[33]

3. Formulation related factors

A. Molecular size

Smaller molecules (75 100 Da) generally exhibit rapid transport across the mucosa, with permeability decreasing as molecular size increases. For hydrophilic macromol ecules such as peptides, absorption enhancers have been used to successfully alter the permeability of buccal epithelium, making this route more suitable for delivery of larger molecules.

B. Partition coefficient

partition coefficient is a useful tool to determine the absorption potential of a drug. I n general, increasing a drug's polarity by ionization or hydroxyl, carboxyl, or amino groups, will increase the water solubility of any particular drug and cause a decrease in lipidwater partition coefficient. Conversely, decreasing the polarity of a drug (e.g. adding methyl or methylene groups) results in an increased partition coefficient and decreased water solubility.

C. pH

partition coefficient is also affected by pH at the site of drug absorption. With incr easing pH, the partition coefficient of acidic drugs decreases while that of basic dr ugs increase. The partition coefficient is also an important indicator of chemical storage in oil field Obese people can store large items Fat soluble drugs found in fat depots. This drug is soluble in lipids and acts as a reservoir for slow release from fatty deposits.

D. pKa

Ionization of the drug is directly related to the pKa and pH of the mucosal surface. Only the nonionized forms of many weak acids and bases show significant lipid solubility and

he nce the ability to cross lipid membranes. Therefore, the maximum absorbance of these compounds occurs at the pH at which they are ionized, and as ionization increases, the absorbance decreases.[33]

Recent Developments in Oral Drug Delivery Systems

In recent years, there has been interest in developing alternative bioadhesive drug formulations for mucus to solve this limitation. Advances in oral delivery of peptides i n BDDS, such as oral lipophilic gels and phospholipid vesicles, have been proposed. Some authors specifically recommend the use of glyceryl monooleate as an oral solu tion for the cubic and layered liquid crystal phase of the peptide.[34] A new liquid a erosol has been developed in the last decade (Oralin)[35] recently developed phosp holipid deformable vesicles for insulin delivery in the oral cavity.[36]

CONCLUSION

The need for drug delivery research is always trying to find and use modern technology increasingly better. This advantage extends the delivery time. The mucosa has v ery good vascular and lymphatic flow, it does not first pass through metabolism in the liver and does not undergo presystemic elimination from the intestine. Moreover, elimination of Drugs in case of toxicity provides a good and easy way of drug use.

REFERENCES

1. Gazzi Shanker, C. K. Kumar, C. S. R. Gonugunta, B. V. Kumar, & P. R. Veerareddy. Formulation and Evaluation of Bioadhesive Buccal Drug Delivery of Tizanidine Hydrochloride Tablets. AAPS PharmSciTech, 2009; 10(2).
2. Squier, C. A., & Wertz, P. W. Structure and function of the oral mucosa and implications for drug delivery. In M. J. Rathbone (Ed.), Oral mucosal drug delivery New York: Marcel Dekker, 1996; 1–2.
3. Gibaldi, M. The number of drugs administered buccally is increasing. Clin Pharmacol, 1985; 3: 49–56.
4. Harris, D., & Robinson, J. R. Drug delivery via the mucous membranes of the oral cavity. J Pharm Sci, 1992; 81: 1–10.
5. Davis, S. S., Daly, P. B., Kennerley, J. W., Frier, M., Hardy, J. G., & Wilson, C. G. Design and evaluation of sustained release formulations for oral and buccal administration. In W. D. Bussmann, R. R. Dries, & W. Wagner (Eds.), Controlled release nitroglycerin in buccal and oral form Basle: Karger, 1982; 17–25.
6. Schor, J. M., Davis, S. S., Nigalaye, A., & Bolton, S. Susadrin transmucosal tablets. Drug Dev Ind Pharm, 1983; 9: (1359–1377).
7. Ishida, M., Nambu, N., & Nagai, T. Mucosal dosage form of lidocaine for toothache using hydroxypropyl cellulose. Chem Pharm Bull, 1982; 30: 980–984.
8. Bremecker, K. D., Strempel, H., & Klein, G. Novel concept for a mucosal adhesive ointment. J Pharm Sci, 1984; 73: 548–552.
9. Anders, R., & Merkle, H. P. Evaluation of laminated mucoadhesive patches for buccal drug delivery. Int J Pharm, 1989; 49: 231–240.
10. Gandhi, R. B., & Robinson, J. R. Bioadhesion in drug delivery. Ind JPharm Sci, 1988; 50: 145–152.
11. Shojaei, A. H. Buccal mucosa as a route for systemic drug delivery: a review. J Pharm Pharmaceut Sci, 1998; 1(1): 15–30.
12. Nagai, T., & Machida, Y. Advances in drug delivery: mucosal adhesive dosage forms. Pharm Int, 1985; 6: 196–200.
13. Chattarajee, S. C., & Walker, R. B. Penetration enhancer classification. In E. W. Smith & H. I. Maibach (Eds.), Percutaneous penetration enhancement Boca Raton: CRC, 1995; 1–4.
14. Aungst, B. J., & Rogers, N. J. Comparison of the effects of various transmucosal absorption promoters on buccal insulin delivery. Int J Pharm, 1989; 53: 227–235.
15. Lee, V. H. L., Yamamoto, A., & Kompella, U. B. Mucosal penetration enhancers for facilitation of peptide and protein drug absorption. Crit Rev Ther Drug Carrier Syst, 1991; 8: 191–192.
16. Pitha, J., Harman, S. M., & Michel, M. E. Hydrophilic cyclodextrin derivatives enable effective oral administration of steroidal hormones. J Pharm Sci, 1986; 75: 165–167.
17. Burnside, B. A., Keith, A. D., & Snipes, W. Microporous hollow fibers as a peptide delivery system via the buccal cavity. In Proc Int Symp Control Release Bioact Mater, 1989; 16: 93–94.
18. Chinna Reddy, P., Chaitanya, K. S. C., & Madhusudan Rao, Y. A review on bioadhesive buccal drug delivery systems: Current status of formulation and evaluation methods. DARU, J Pharm Sci., 2011; 19(6): 385-403.
19. Hao, J., & Heng, P. W. S. Buccal delivery systems. Drug Dev Ind Pharm., 2003; 29(8): 821-832. doi:10.1081/DDC-120024178
20. Buccal Drug Delivery System: A Review. Institute of Pharmaceutical Sciences, Kurukshetra University, Kurukshetra, Haryana, India.
21. Andrews, G. P., Laverty, T. P., & Jones, D. S. Mucoadhesive polymeric platforms for controlled drug delivery. Eur J Pharm Biopharm, 2009; 71(3): 505-518. doi:10.1016/j.ejpb.2008.09.028
22. Khairnar, G. A., & Sayyad, F. J. Development of buccal drug delivery system based on mucoadhesive polymer. International Journal of Pharm Tech Research, 2010; 2(1): 719-735.
23. Bruschi, M. L., & De Freitas, O. Oral bioadhesive drug delivery systems. Drug Dev Ind Pharm, 2005; 31(3): 293-310. doi:10.1081/DDC-52073
24. Irache, J., Huici, M., Konecny, M., Espuelas, S., Campanero, M., & Arbos, P. Bioadhesive Properties of Gantrez Nanoparticles. Molecules, 2005; 10(1): 126-145. doi:10.3390/10010126
25. Hassan, E. E., & Gallo, J. M. (Undated). A Simple Rheological Method for the in Vitro Assessment of Mucin-Polymer Bioadhesive Bond Strength. Pharm Res An Off J Am Assoc Pharm Sci. (Note: The

provided text appears incomplete; please provide more details or verify the information.)
26. Salamat-Miller, N., Chittchang, M., & Johnston, T. P. The use of mucoadhesive polymers in buccal drug delivery. Advance Drug Delivery Review, 2005; 57(11): 1666-1691.
27. Sheoran, R. (Undated). Buccal drug delivery system. Institute of Pharmaceutical Sciences, Kurukshetra University, Kurukshetra, Haryana, India.
28. Reddy, R. J., Anjum, M., & Hussain, M. A. (Undated). A Comprehensive Review on Buccal Drug Delivery System. (Note: The provided text appears incomplete; please provide more details or verify the information.)
29. Rao, N. G. R., Shravani, B., & Reddy, S. M. Overview on Buccal Drug Delivery Systems. J Pharm Sci Res., 2013; 5(4): 80-88.
30. Budhrani, A., & Shadija, A. K. Mucoadhesive buccal drug delivery system: A review. Am J Pharmtech Res., 2020; 10(2): 274-285. doi:10.46624/ajptr.2020.v10.i2.020
31. Mohit, & Hussain, M. S. (Undated). A BRIEF REVIEW ON BUCCAL DRUG DELIVERY SYSTEM: ADVANTAGES, LIMITATIONS, AND IMPACT ON HEALTHCARE SYSTEM. School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, 144411, Punjab, India.
32. Puratchikody, A., Prasanth, V. V., Mathew, S., & Balaraman, A. K. Buccal Drug Delivery: Past, Present and Future – A Review. Int J drug Deliv, 2011; 3(2): 171-184.
33. Gandhi, P. A., Patel, K. R., Patel, M. R., & Patel, N. M. A Review Article on Mucoadhesive Buccal Drug Delivery System. Inter. J. of Pharm. Res. Development, 2011; 3(5): 159-173.
34. Lee, J., & Kellaway, I. W. Buccal permeation of [D-Ala2, D- Leu5]enkephalin from liquid crystalline phases of glyceryl monooleate. Int J Pharm., 2000; 195(1-2): 35-38. doi:10.1016/S0378-5173(99)00357-9
35. Modi, P., Mihic, M., & Lewin, A. The evolving role of oral insulin in the treatment of diabetes using a novel RapidMistTM system. Diabetes Metab Res Rev., 2002; 18(1). doi:10.1002/dmrr.208
36. Yang, T. Z., Wang, X. T., Yan, X. Y., & Zhang, Q. Phospholipid deformable vesicles for buccal delivery of insulin. Chem Pharm Bull, 2002; 50(6): 749-753. doi:10.1248/cpb.50.749