BUCCAL ROUTE DELIVERY: A FRUITFUL TOOL FOR PHARMACEUTICALS

Garaga Shirisha, Rubina Apsar Shaik
Bojjam Narasimhulu Pharmacy College For Women, Vinaynagar, Hyderabad
e-mail ID: gvasirisha@yahoo.com

ABSTRACT: The buccal region of the oral cavity is an attractive target for administration of the drug of choice, particularly in overcoming deficiencies associated with the latter mode of administration. Problems such as high first-pass metabolism and drug degradation in the gastrointestinal environment can be circumvented by administering the drug via the buccal route. Moreover, rapid onset of action can be achieved relative to the oral route and the formulation can be removed if therapy is required to be discontinued. It is also possible to administer drugs to patients who unconscious and less co-operative. To prevent accidental swallowing of drugs adhesive mucosal dosage forms were suggested for oral delivery, which included adhesive tablets, adhesive gels, adhesive patches and many other dosage forms with various combinations of polymers, absorption enhancers. Natural polymers have recently gained importance in pharmaceutical field. The substrate possessing bioadhesive polymer can help in drug delivery for a prolonged period of time at a specific delivery site.

Keywords: Mucoadhesive buccal patch, Natural polymer, Bioadhesive polymers, Buccal formulations, Buccal Mucosa, first-pass effect, permeation enhancers.

I. INTRODUCTION

The unique environment of the oral cavity offers its potential as a site for drug delivery. Because of the rich blood supply and direct access to systemic circulation, the oral mucosal route is suitable for drugs, which are susceptible to acid hydrolysis in the stomach or which are extensively metabolized in the liver (first pass effect). The total area of the oral cavity is about 100 cm². Out of this about one third is the buccal surface, which is lined with an epithelium of about 0.5 mm thickness. The oral mucosal surface is constantly washed by the saliva (daily turn out is about 0.5 to 2 liters). The continuous secretion of saliva results in rapid removal of released drug. Conversely, the thin mucin film, which exists on the surface of the oral mucosa, may provide an opportunity to retain a drug delivery system in contact with the mucosa for prolonged periods if it is designed to be mucoadhesive. Such systems ensure a close contact with absorbing membrane, thus optimizing the drug concentration gradient across the biological membrane and reducing the differential pathway. Therefore, the buccal (oral) mucosa may be a potential site for controlled or sustained drug delivery. Drug delivery via the membranes of the oral cavity is traditionally divided into three categories, buccal delivery - which infers drug administration through the lining of the cheek to the systemic circulation, sublingual delivery - which infers drug administration through the administration of drug via membranes of the floor of the mouth for the systemic circulation, local delivery to mouth - which involves treatment conditions with in the oral cavity by administration to the affected mucosal tissues. These sites for delivery differ in both structure and composition as well as in degree of permeability and therefore, also vary in their ability to retain a delivery for a desired length of time. Buccal route of drug delivery is a good alternative among the various routes of drug delivery. However, preoral 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 mucosa are considered as potential sites for drug administration. Over the last two decades mucoadhesion has become of interest for its systemic delivery by retaining a formulation intimate contact with buccal cavity. The term bio adhesion has been used to define the attachment of a synthetic natural macromolecule to a biological tissue for an extended period of time. When a substrate of mucosal system adheres and interacts primarily with the mucus layer, this phenomenon being referred to as mucoadhesion. The adhesive properties of such drug delivery platforms can reduce the enzymatic degradation due to the increased intimacy between the delivery vehicle and the absorbing membrane. The use of mucoadhesive polymers in buccal drug delivery has a greater application. 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. Buccal route of drug delivery provides the direct access to the systemic circulation through the jugular vein bypassing the first pass hepatic metabolism leading to high bioavailability.

Advantages: Bypass of the gastrointestinal tract and hepatic portal system, increasing the bioavailability of orally
administered drugs that otherwise undergo hepatic first metabolism. Improved patient compliance due to the elimination of associated pain with injections; administration of drugs in unconscious or incapacitated patients.sustained release of drug.A relatively rapid onset of action can be achieved relative to the oral route, and the formulation can be removed if therapy is required to be discontinued. Increased ease of drug administration. Disadvantages 10 Drugs which irritate the oral mucosa, have better or unpleasant odour cannot be administered by this route. Only drugs with small dose requirements can be administered. Only those drugs which are absorbed by passive diffusion can be administered by this route. Swallowing of saliva can also potentially lead to the loss of dissolved or suspended drug and ultimately the involuntary removal of the dosage form.

Fig. 1. Oral cavity

The various strategies Employed for Buccal Delivery Bioadhesive Buccal Tablets, Bioadhesive buccal Gels, Bioadhesive Buccal Patches

A. Bioadhesive Buccal Tablet: Bioadhesive tablets are immobilized drug delivery systems. They can be formulated into monolithic, partially coated or multi-layered matrices. Monolithic tablets are easy to manufacture by conventional techniques and provide the possibility of loading large amount of drug. In case of bi-layered tablets, drug can be incorporated in the adhesive layer, which comes in contact with the mucosal surface. The drug containing mucoadhesive layer is then protected from the oral cavity environment by a super upper inert layer (backing layer), which faces into the oral cavity.

B. Bioadhesive Buccal Patches: Adhesive patches can be designed either for unidirectional release into the oral mucosa or for bi-directional release into the oral cavity as well as into the oral mucosa. The adhesive part of the system can be used as drug carrier or as an adhesive for the retention of a drug loaded non-adhesive layer. In this respect, a peripheral adhesive ring should be casted. The use of an impermeable backing layer will maximize the drug concentration gradient and prolong adhesion because the system is protected from saliva.

C. Bioadhesive buccal Gels: Viscous adhesive gels have been designed for local therapy using polyacrylic acid and polymethacrylate as gel forming polymers. Gels are reported to prolong residence time on the oral mucosa to a significant level. This not only improves absorption but also allows for sustained release of the active principle. Structure and design of Buccal Dosage Form: Drug delivery designed for the buccal mucosa contains a polymeric adhesive component. When in contact with the saliva, the adhesive attaches to the mucosa causing immediate and rapid drug delivery. Trans mucosal drug delivery systems can be unidirectional or bi-directional. Unidirectional patches release the drug only into the mucosa, while bi-directional patches release the drug in both the mucosa and the mouth. The buccal patch is designed in either a matrix configuration with drug, adhesive, and additives mixed together, or a reservoir system that contains a cavity for the drug and additives separate from the additives. An impermeable backing is applied to control the direction of drug delivery, to reduce patch deformation and disintegration while in the mouth and to prevent drug loss. Additionally, the patch can be
constructed to undergo minimal degradation in the mouth or can be designed to dissolve immediately.¹⁶

**Fig.2 and 3.** Structural features of oral cavity.

**Buccal dosage form for buccal delivery:**

1. **Matrix type:** The buccal patch designed in a matrix configuration contains drug, adhesive, and additives mixed together.

2. **Reservoir type:** The buccal patch designed in a reservoir system contains a cavity for the drug and additives separate from the adhesive. An impermeable backing is applied to control the direction of drug delivery, to reduce patch deformation and disintegration while in the mouth and to prevent drug loss. Additionally, the patch can be constructed to undergo minimal degradation in the mouth, or can be designed to dissolve almost immediately.¹⁸

**Fig.4.** Design of matrix type patch

**Fig.5.** Design of reservoir type of patch

**Mechanism of buccal absorption:** Buccal drug absorption occurs by passive diffusion of the nonionized species, a process governed primarily by a concentration gradient, through the intercellular spaces of the epithelium. The passive transport of non-ionic species across the lipid membrane of the buccal cavity is the primary transport mechanism.¹⁹ The buccal mucosa has been said to be a lipoidal barrier to the passage of drugs, as is the case with many other mucosal membrane and the more lipophilic the drug molecule, the more readily it is absorbed. The dynamics of buccal absorption of drugs could be adequately described by first order rate process. Several potential barriers to buccal drug absorption have been identified. Dearden and Tomlison (1971) pointed out that salivary secretion alters the buccal absorption kinetics from drug solution by changing the concentration of drug in the

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mouth.

III METHOD OF PREPARATION

1. Solvent casting: In this, all patch excipients including the drug is 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. The solvent casting method is simple, but suffers from some disadvantages, including long processing time, high cost and environmental concerns due to the solvents used. These drawbacks can be overcome by the hot-melt extrusion method.

2. Direct milling: In this patches are manufactured without the use of solvents (solvent-free). 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. An impermeable backing membrane may also be applied to control the direction of drug release, prevent drug loss, and to minimize deformation and disintegration of the device during application period. While there are only minor or even no differences in patch performance by between patches are fabricated with the two processes, the solvent-free process is preferred because there is no possibility of residual solvents and no associated solvent-related health issues.

IV BIOADHESIVE POLYMERS

In the large classes of hydrophilic polymers those containing carboxylic group exhibit the best mucoadhesive properties. Polyvinylpyrrolidone (PVP), methyl cellulose (MC), sodium carboxy methyl cellulose (SCMC), Hydroxyl propyl cellulose (HPC) and other cellulose derivatives. Hydrogels are the class of polymeric biomaterial that exhibit the basic characteristics of an hydrogels to swell by absorbing water interacting by means of adhesion with the mucus that covers epithelia i.e. 31

- Anionic group --- Carbopol, Polyacrylates and their cross linked modifications.
- Cationic group --- Chitosan and its derivatives
- Neutral group --- Eudragit-NE30D etc.

Important Factors of Buccoadhesion

- High molecular weight (up to 100000)  
- High viscosity Long chain polymers
- Optimum concentration of polymeric adhesive, Flexibility of polymer chain, Spatial confirmation, Optimum cross-linked density of polymer, charge and degree of ionization of polymer (anion > action > unionized),Optimum medium pH.  
- Optimum hydration of the polymer and high applied strength and duration of its application and high initial contact time are some basic properties which a polymer must have to show for good mucoadhesive profile. Besides the above factors, some physiological factors like mucin turnover and disease
status also affect the Buccoadhesion. The mucin turnover is expected to limit the residence time of the buccoadhesives on the buccal mucosa. No matter, how high the buccoadhesive strength, buccoadhesives are detached from the surface due to mucin turnover. The physiochemical properties of the mucus are known to change during disease conditions such as cold, bacterial and fungal infections and inflammatory conditions, there by changing the degree of buccoadhesion.

V CONCLUSION

Based on review conclude that it is necessary not only to develop new drugs but also to optimise the different routes of administration so as to increase the effectiveness and minimise the side effects.

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