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A REVIEW ON TRANSMUCOSAL DRUG DELIVERY SYSTEM: AN INNOVATIVE APPROACH

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ABSTRACT

"The successful delivery of drugs across the oral mucosa represents a continuing challenge, as well as a great opportunity". Oral transmucosal delivery, especially buccal and sublingual delivery, has progressed far beyond the use of traditional dosage forms with novel approaches emerging continuously. This review highlights the physiological challenges as well as the advances and opportunities for transmucosal drug delivery within the oral mucosal cavity by discussing the structure and environment of the oral mucosa and the experimental methods used in assessing buccal drug permeation or absorption also to study about novel Mucoadhesive polymers and to design improved drug delivery systems forms in efforts to achieve systemic delivery of drugs through the different mucosa. Th transmucosal drug delivery system is a popular novel drug delivery method because mucous membranes are relatively permeable, allowing for the rapid uptake of a drug into the systemic circulation and avoiding the first pass metabolism. Mucoadhesive polymers have been utilized in much different dosage which includes tablets, patches, tapes, films, semisolids and powders. These dosage forms include tablets, patches, tapes, films, semisolids and powders. Buccal dosage forms will also be reviewed with an emphasis on bioadhesive polymeric based delivery systems.

KEYWORDS: Transmucosal, Mucoadhesive polymer, buccal tablet, nanosponges, systemic delivery.

INTRODUCTION

The cost involved both in terms of money and time in the development of a single new chemical entity has made it mandatory for pharmaceutical companies to reconsider delivery strategies to improve the efficacy of drugs that have already been approved.

However, despite the tremendous advances in drug delivery, the oral route remains the preferred route for the administration of therapeutic agents due to low cost, ease of administration and high level of patient compliance but in spite of that, significant barriers impose for the peroral administration of drugs, such as hepatic first pass metabolism and drug degradation within the gastrointestinal (GI) tract prohibiting the oral administration of certain classes of drugs especially biologics e.g. peptides and proteins.

Consequently, other absorptive mucosa are being considered as potential sites for drug administration including the mucosal linings of the nasal, rectal, vaginal, ocular, and oral cavity. These transmucosal routes of drug delivery offer distinct advantages over peroral administration for systemic drug delivery such as possible bypass of the first pass effect and avoidance of presystemic elimination within the GI tract.[1-2]

Amongst these, delivery of drugs to the oral cavity has attracted particular attention due to its potential for high patient compliance and unique physiological features.

Within the oral mucosal cavity, the delivery of drugs is classified into two categories:
-Local delivery.
-Systemic delivery either via the buccal or sublingual mucosa.

This review examines the physiological considerations of the oral cavity in light of systemic drug delivery and provides an insight into the advances in oral transmucosal delivery systems.

The emerging technique of combinatorial chemistry, along with a growing knowledge of the biochemistry of the human body, has lead to an ever-increasing number of therapeutic Proteins in the treatment of diseases; however, these proteins often lack durability that more traditional small molecule pharmaceutics possess.

Where a simple therapeutic agent, such as aspirin or simple antibiotic, can be taken orally and reach the bloodstream intact, the larger and more delicate protein must often be delivered directly into the bloodstream through injection.

The harsh conditions of the stomach often destroy a vast majority of the protein before it reaches the bloodstream.

In the case of insulin, less than 0.1% of the orally dosed insulin reaches the blood stream intact.[4]

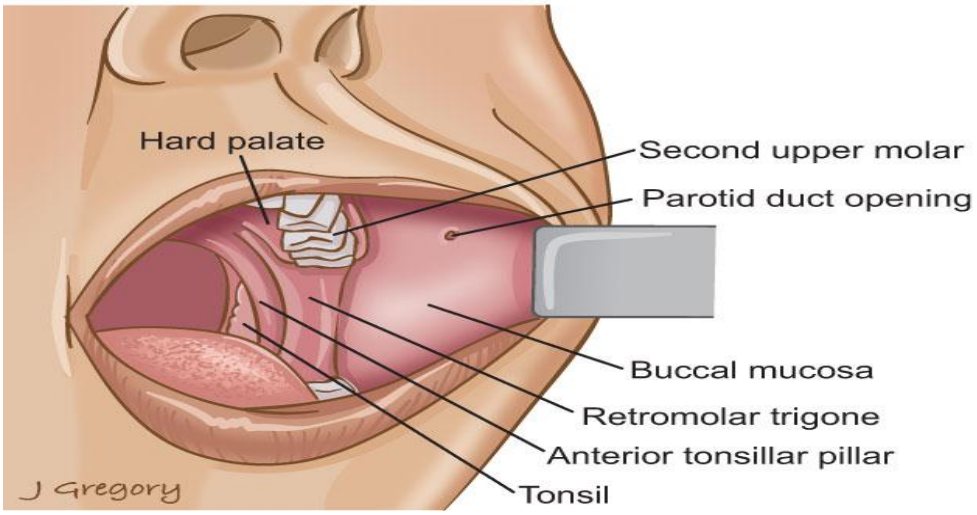

Figure 1: Schematic representation of oral mucosa[3]

OBJECTIVES

This review is to study about novel Mucoadhesive polymers and to design improved Drug delivery systems, as it evades first-pass metabolism, enhances drug bioavailability and provides the means for rapid drug transport to the systematic circulation.[4]

This delivery system offers a more comfortable and convenient delivery route compared with the intravenous route.

Although numerous drugs have been evaluated for oral mucosal delivery, few of them are available commercially.

This is due to limitations such as the high costs associated with developing such drug delivery systems.[4]

ANATOMY AND PHYSIOLOGY OF ORAL MUCOSA

Light microscopy reveals several distinct patterns of maturation in the epithelium of the human oral mucosa based on various regions of the oral cavity. Three distinctive layers of the oral mucosa are the epithelium, basement membrane, and connective tissues. The oral cavity is lined with the epithelium, below which lies the supporting basement membrane. The basement membrane is supported by connective tissues.

The epithelium, as a protective layer for the tissues beneath, is divided into, non-keratinized surface in the mucosal lining of the superior labia, soft palate, hard palate, palatine tonsils, inferior vestibule, the ventral surface of the tongue, the floor of the mouth, alveolar mucosa, vestibule, lips, and cheeks, Keratinized epithelium which is found in the hard palate and non-flexible regions of the oral cavity.

The epithelial cells, originating from the basal cells, mature, change their shape, and increase in size while moving towards the surface.

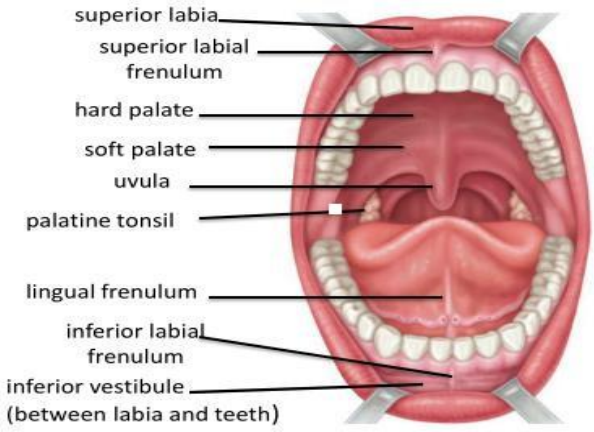

Figure 2. Anatomy of Oral Mucosa. (www.slideserve.com)[3]

The basement membrane forms a distinctive layer between the connective tissues and the epithelium.

It provides the required adherence between the epithelium and the underlying connective tissues, and functions as a mechanical support for the epithelium.

The buccal epithelium is classified as a non-keratinized tissue. It is penetrated by tall and conical-shaped connective tissues.
A gel-like secretion known as mucus, which contains mostly water-insoluble glycoproteins, covers the entire oral cavity.

Mucus is bound to the apical cell surface and acts as a protective layer to the cells below.
It is also a visco-elastic hydrogel, and primarily consists of 1-5% of the above-mentioned water insoluble glycoproteins, 95-99% water, and several other components in small

quantities, such as proteins, enzymes, electrolytes, and nucleic acids. This composition can vary based on the origin of the mucus secretion in the body.[4-5]

OVERVIEW OF ORAL MUCOSA

The anatomical and physiological properties of oral mucosa had been extensively reviewed by several authors. The oral cavity comprises the lips, cheek, tongue, hard palate, soft palate and floor of the mouth. The lining of the oral cavity is referred to as the oral mucosa, and includes the buccal, sublingual, gingival, palatal and labial mucosa. The buccal, sublingual and the mucosal tissues at the ventral surface of the tongue accounts for about 60% of the oral mucosal surface area. The top quarter to one-third of the oral mucosa is made up of closely compacted epithelial cells. The primary function of the oral epithelium is to protect the underlying tissue against potential harmful agents in the oral environment and from fluid loss. Beneath the epithelium are the basement membrane, lamina propria and submucosa. The oral mucosa also contains many sensory receptors including the taste receptors of the tongue.[4] they also contain following parameter.

A. Structure.

B. Permeability.

C. Environment.

A. Structure

The oral mucosa is composed of an outermost layer of stratified squamous epithelium below this lies a basement membrane, a lamina propria followed by the submucosa as the innermost layer. The epithelium is similar to stratified squamous epithelia found in the rest of the body in that it has a mitotically active basal cell layer, advancing through a number of differentiating intermediate layers to the superficial layers, where cells are shed from the surface of the epithelium.

The epithelium of the buccal mucosa is about 40-50 cell layers thick, while that of the sublingual epithelium contains somewhat fewer.

The epithelial cells increase in size and become flatter as they travel from the basal layers to the superficial layers.[5]

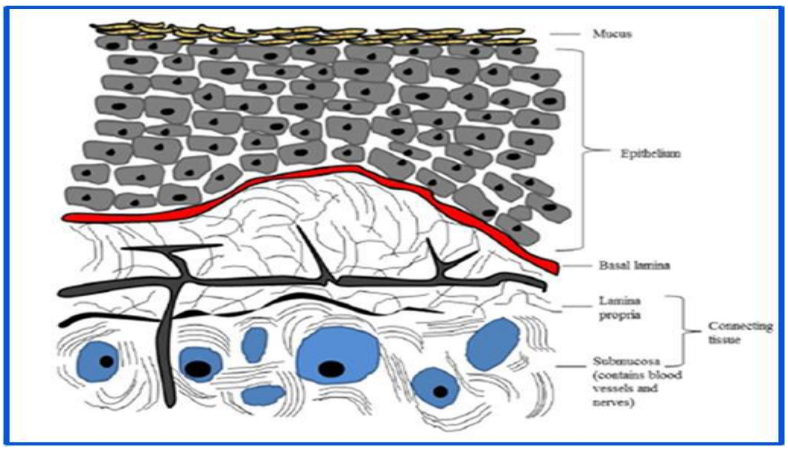

Figure 3: Structure of oral mucosa.[5]

B. Permeability

The oral mucosa in general is somewhat leaky epithelia intermediate between that of the epidermis and intestinal mucosa.

It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of the skin.

As indicative by the wide range in this reported value, there are considerable differences in permeability between different regions of the oral cavity because of the diverse structures and functions of the different oral mucosa.

In general, the permeability of the oral mucosa decreases in the order of sublingual greater than buccal and buccal greater than palatal. This rank order is based on the relative thickness and degree of keratinization of these tissues, with the sublingual mucosa being relatively thin and non-keratinized, the buccal thicker and non-keratinized, and the palatal intermediate in thickness but keratinized.

It is currently believed that the permeability barrier in the oral mucosa is a result of intercellular material derived from the so-called ‘membrane coating granules’ (MCG).

When cells go through differentiation, MCGs start forming and at the atypical cell surfaces they fuse with the plasma membrane and their contents are discharged into the intercellular spaces at the upper one third of the epithelium.[4-5]

It is estimated that 25% of the population finds it difficult to swallow tablets and capsules and therefore do not take their medication as prescribed by their doctor resulting in high incidence of non-compliance and ineffective therapy.[5-6]

C. Environment

The cells of the oral epithelia are surrounded by an intercellular ground substance, mucus, the principle components of which are complexes made up of proteins and carbohydrates.

These complexes may be free of association or some maybe attached to certain regions on the cell surfaces.

This matrix may actually play a role in cell-cell adhesion, as well as acting as a Lubricant, allowing cells to move relative to one another.

Along the same lines, the mucus is also believed to play a role in bioadhesion of Mucoadhesive drug delivery systems.

In stratified squamous epithelia found elsewhere in the body, mucus is synthesized by specialized mucus secreting cells like the goblet cells, however in the oral mucosa; mucus is secreted by the major and minor salivary glands as part of saliva.

Up to 70% of the total mucin found in saliva is contributed by the minor salivary glands At physiological pH the mucus network carries a negative charge (due to the sialic acid and sulfate residues) which may play a role in mucoadhesion.

At this pH mucus can form a strongly cohesive gel structure that will bind to the epithelial cell surface as a gelatinous layer.

Saliva is an aqueous fluid with 1% organic and inorganic materials.

The major determinant of the salivary composition is the flow rate which in turn depends upon three factors

1. Time of day.
2. Type of stimulus.
3. Degree of stimulation.

The salivary pH ranges from 5.5 to 7 depending on the flow rate. At high flow rates, the sodium and bicarbonate concentrations increase leading to an increase in the pH.

The daily salivary volume is between 0.5 to 2 liters and it is this amount of fluid that is available to hydrate oral mucosal dosage forms.

A main reason behind the selection of hydrophilic polymeric matrices as vehicles for oral transmucosal drug delivery systems is this water rich environment of the oral cavity.[6-7]

PHYSIOLOGICAL BARREIERS OF TRANSMUCOSAL DRUG DELIVERY SYSTEM

The environment of the oral cavity presents some significant challenges for systemic drug delivery. The drug needs to be released from the formulation to the delivery site (e.g. buccal or sublingual area) and pass through the mucosal layers to enter the systemic circulation.

Certain physiological aspects of the oral cavity play significant roles in this process, including pH, fluid volume, enzyme activity and the permeability of oral mucosa.

For drug delivery systems designed for extended release in the oral cavity (e.g. mucodhesive systems), the structure and turnover of the mucosal surface is also a determinant of performance.[7]

a) Buccal cavity.
b) Vagina.
c) Nasal cavity.
d) Eye.
e) Gastrointestinal tract.

a) Buccal cavity

At this site, first-pass metabolism is avoided, and the non-keratinized epithelium is relatively permeable to drugs.

Due to flow of saliva and swallowing, materials in the buccal cavity have a short residence time and so it is one of the most suitable areas for the development of bioadhesive devices that adhere to the buccal mucosa and remain in place for a considerable period of time.[7]

b) Vagina

The vagina is a highly suitable site for bioadhesive formulations and it is here that the success of the concept can be seen convincingly.

The bioadhesion increases the retention time (up to 72 h) and a smaller amount of the active ingredient can be used, reducing any adverse effects.[7]

c) Nasal cavity

Ease of access, avoidance of first-pass metabolism and a relatively permeable and well-vascularised membrane, contribute to make the nasal cavity an attractive site for drug delivery.[6-7]

d) Eye

One major problem for drug administration to the eye is rapid loss of the drug and or vehicle as a result of tear flow, and so it is a target for prolonging the residence time by bioadhesion.[7]

e) Gastrointestinal tract

The gastrointestinal tract has been the subject of intense study for the use of bioadhesive formulations to improve drug bioavailability. The problem associated is that the polymeric bioadhesive formulations bind the intestinal mucus, which is constantly turning over and are transported down the gut by peristalsis. Another problem is that with conventional formulations such as tablets, the active ingredient may diffuse relatively rapidly away from the bioadhesive.[8]

PHARMACUETICAL CONSIDERATIONS AND FORMULATIONS DESIGN FOR SUCCESSFUL TRANSMUCOSAL DRUG DELIVERY SYSTEM:

1) **Patches.**
2) **Solution gels.**
3) **Buccal tablet.**
4) **Films.**
5) **Nanosponges.**

1) Patches

Flexible adhesive patches have been developed in an effort to overcome some of the drawbacks of other dosage forms.

Transmucosal delivery patches have unique characteristics, including relatively rapid onset of drug delivery, sustained drug release and rapid decline in the serum drug concentration when the patch is removed.

Also, a buccal patch is confined to the buccal area over which it is attached and therefore the absorption profile may have less inter- and intra individual variability.

In general, oral mucosal patches can be classified into three categories: patches with a dissolvable matrix, patches with a non-dissolvable backing, and patches with a dissolvable backing. Patches with a dissolvable matrix are designed to release drug into the oral cavity.

The Mucoadhesive layer, either in the drug matrix or attached to drug matrix as an additional layer, prolongs the duration of drug matrix in the oral cavity.

Therefore, compared with other open dosage forms, these types of patches are longer acting and can potentially deliver more drugs.

They also use the entire oral cavity mucosa as compared with other closed systems that typically use smaller areas. These types of patches are also suitable for treating local diseases such as candidacies or mucositis.

Patches with non-dissolvable backing are usually designed for systemic delivery. Since they are closed systems and the formulations are protected from saliva, the drug concentrations are controlled and drug is continuously delivered for 10 to 15 h.[6,7]

Composition of buccal patches

A. Active ingredient.

B. Polymers (adhesive layer)

HEC, HPC, polyvinyl pyrrolidone(PVP), polyvinyl alcohol (PVA), carbopol and other mucoadhesive polymers.

C. Diluents

Lactose DC is selected as diluents for its high aqueous solubility, its flavoring characteristics, and its physico-mechanical properties, which make it suitable for direct Compression.

Other example: microcrystalline starch and starch.

D. Sweetening agents

Sucralose, aspartame, Mannitol, etc.

E. Flavoring agents

Menthol, vanillin, clove oil, etc.

F. Backing layer

EC etc.

G. Penetration enhancer

Cyano acrylate, etc.

H. Plasticizers

PEG-100, 400, propylene glycol, etc.[6-8]

Evaluation of patches

- **Mass uniformity and thickness of patches**

Mass uniformity and thickness (selected buccal patches) was done for randomly selected ten Individual patches. The thickness and mass uniformity is measured by using screw gauge and digital weighing balances carefully.

- **Folding endurance**

The folding endurance of randomly selected patches (without backing membrane) was Determined by repeatedly folding one patch at the same place till it break or folded maximum 250 times.

- **Drug content uniformity**

Aceclofenac buccal patches are allowed dissolve in 10 ml of simulated saliva pH, under Occasional shaking for 3 hr, withdraw 2 ml sample solution filter with filter paper after that Suitable dilutions was made and amount of drug present in per patch was determined by using UV spectrometer (Shimadzu 1800, Japan) at 272nm.

- **Measurement of surface pH**

Buccal patches were placed on the surface of agar plate (the agar plate is prepared by dissolving Agar 2% w/v in warmed phosphate buffer pH 6.2 under stirring then poured to Petridish to Solidify at room temperature allow swelling for some time. The surface pH is

measured bringing a glass electrode in contact with surface of the patch and allow to equilibrate for 1 min. Averages of three readings are recorded.

- **Swelling studies**

The weight of the patch, without backing membrane was determined by digital electronic Weighing balance. Patches are placed on the surface of an agar plate and allowed to swell by Keeping it an incubator at 37 ºC and the diameter is measured at predetermined time intervals for 90 minutes.

Swelling index was calculated from following equation,

Swelling index = (W2- W1 / W1) ×100

Where SI (%) is percent swelling, W2 is the swollen patch weight, W1 is the initial weight of the Patch.[7-8]

2) Solutions gels

Viscous liquids have been investigated primarily to coat the mucosa to act as a protectant or a vehicle for drug delivery for the treatment of local disorders, including motility dysfunction, fungal infections.

Both polycarbophil and xanthan gum demonstrated excellent bioadhesive potential, and carmellose sodium and thermo sensitive poloxamer (Lutrol 407) demonstrated poor Retention.

A thermo sensitive hydrogel of poloxamer covalently linked to polyacrylic acid and carbopol. This "esophageal bandage", upon oral administration, demonstrated significant retention within the esophagus.[7-9]

3) Buccal tablet

The transmucosal tables are intended to be held in the mouth, where they release their drug contents for absorption directly through the oral mucosa.

The nitroglycerin sublingual and prochlorpromazine buccal tablets are most commonly used formulations, available in market.

The limitation of this delivery form is the short residence time and usually dissolved within 30 min, thus limiting the total amount of drug that can be delivered.

These delivery systems have some limitations such as, inter- and intra-individual variation in absorption and bioavailability because it is difficult to control drug or other ingredient concentrations, as the media is constantly diluted by saliva.

Taste of the drug is another problem for this delivery system if the drug is unpleasant in taste. In this condition, the taste can be masked by sweetening and flavorings agents.

E.g. Shanker et al. studied the formulation and evaluation of bioadhesive buccal drug delivery of tizanidine hydrochloride tablets, which is extensively metabolized by liver.

The tablets were prepared by direct compression using bioadhesive polymers such as hydroxyl propyl methylcellulose K4M, sodium carboxymethyl cellulose alone and a combination of these two polymers.[8,9]

4) Films

Transmucosal films systems have several unique features, which include relatively rapid onset of drug delivery, sustained drug release, rapid decline in the serum drug concentration when the patch is removed and less inter- and intra-individual variability.

Since they are closed systems and the formulations are protected from saliva, the drug concentrations are controlled and drug is continuously delivered for 10-15 h.

These systems have some limitations such as, they use only a small mucosal area and the backings have to be removed by the patient after drug administration.

Eg. Thimmasetty et al. prepared a carvedilol (b-adrenergic antagonist) patches using hydroxyl propyl methyl cellulose (HPMC), carbopol (CP).

Bioavailability from optimized buccal patch was found 1.46 times higher than the oral dosage form.

Pharmacokinetic studies of the buccal mucoadhesive film showed that the drug was released locally at the target site of action, and a very small amount might have absorbed systemically.

In that fast dissolving film is most acceptable and accurate oral dosage form which bypass the hepatic system and show more therapeutic response.[7, 8, 9]

5) Nanosponges

The system, known as "nanosponge," uses a nanoparticle-sized system to deliver the drug payload.

“Nanosponges” perceived important invention in the field representing versatile activities of β-cyclodextrins, anodic Tio2 forming their layers which will provide a base to deliver both hydrophilic and hydrophobic compounds, Nanosponges had offered an excellency in forming the content having reduced side effects provided with adequacy in improving stability, formulation flexibility.[10]

Nanosponges provide excellent topical delivery of drugs.

Nanosponges embraces nanotechnology which is applied to pharmacy as nanomaterials, diagnosing and focusing right place in the body and controlling release of the drug.

Nanosponges is about the size of virus which has been backed by naturally degradable polyster.[11]

Preparation method of nanosponges [10-12]

A) Solvent Method

Dissolve the polymer in suitable solvent. Then add this to excess quantity of cross- linker.
Reflux the mixture for 48 hours at a temperature of 10oC.
Then allow this solution to cool at room temperature.
Add this to excess quantity of distilled water and filter the product.
Then purify by prolonged soxhlet extraction with ethanol.
Dry the product and grind in mechanical mill to get homogenous powder.

B) From Hyper Cross- Linked B- Cyclodextrins

Here, β- cyclodextrin (β- CD) can be used as carrier for drug delivery.
Nanosponges can be obtained by reacting cyclodextrin with a cross- linker.
Nanosponges can be synthesized in neutral or acid forms.

C) Ultrasound- Assisted Synthesis

In this method, polymers react with cross- linkers in absence of solvent and under sonication. Here, mix the Polymer and cross- linker in a flask.

Place the flask in an ultrasound bath filled with water and heat it to 90oC and Sonicate for 5 hours. Allow it to cool and wash with water to remove the unreacted polymer.

D) Emulsion Solvent Diffusion Method

Nanosponges can be prepared by using ethyl cellulose (EC) and polyvinyl alcohol (PVA).
Ethyl cellulose is dissolved in dichloromethane.
Add this mixture into aqueous solution of polyvinyl alcohol.
Stir the mixture at 1000 rpm for 2 hours in a magnetic stirrer.
Then filter the product and dry it in an oven at 40oC for 24 hours.

Advantages of nanosponges

1) This technology provides entrapment of active contents and side effects are less.
2) It provides improved stability, elegance and formulation flexibility.
3) It is non-mutagenic.
4) Non-irritating, non-toxic.
5) It provides extended release condition which is continuous action up to 12hr.
6) Drug is protected from degradation.

BIOADHESIVE POLYMER USED IN TRANSMUCOSAL DRUG DELIVERY SYSTEM

The ideal bioadhesive polymers should posses some necessary structural characteristics for bioadhesion such as strong hydrogen bonding groups, strong anionic or cationic charges, High molecular weight, chain flexibility and surface energy properties favoring spreading on mucus layer.[12]

Bioadhesive polymer	Objectives
HPC and CP	Preferred mucoadhesive strength on CP, HPC, and HPCCP Combination.
HPC and CP	Measured Bioadhesive property using mouse peritoneal Membrane.
HPC	Formulation and evaluation of Mucoadhesive controlled Released.
CP, PIP, and PIB	Used a two roll milling method to prepare a new Bioadhesive patch formulation livery system.

Hyaluronic acid benzyl esters, Polycarbophil, and HPMC	Evaluate Mucoadhesive properties.
Poly(acrylic acid)	Effects of PAA molecular weight and cross linking concentration on swelling and drug release Characteristics.
Poly(acrylic acid-co-poly Ethylene glycol) copolymer of acrylic acid and poly ethylene glycol monomethyl-ether monomethacryalate.	To enhance the Mucoadhesive properties of PAA for Buccal mucoadhesive drug delivery.

NOVEL MUCOADHESIVE POLYMER

The novel polymers are capable of forming covalent bonds with the mucus and the underlying cell layers, and hence, exhibit improved chemical interactions.

The new generation of mucoadhesives, except thiolated polymers, can adhere directly to the cell surface, rather than to mucus.[12]

(I) Synthetic polymers

1. Cellulose derivatives.. Methylcellulose (MC), Ethyl cellulose (EC), hydroxy ethyl cellulose (HEC), Hydroxyl propyl cellulose (HPC), Sodium carboxy methylcellulose (NaCMC).
2. Poly (Acrylic acid) polymers (Carbomers, Polycarbophil).
3. Poly hydroxyl ethyl methylacrylate.
4. Poly ethylene oxide.
5. Poly vinyl pyrrolidone.
6. Poly vinyl alcohol.

(II) Natural polymers

1. Tragacanth.
2. Sodium alginate.
3. Guar gum.
4. Xanthan gum.
5. Soluble starch.
6. Gelatin.
7. Chitosan.[11-12]

ADVANTAGES OF TRANSMUCOSAL DRUG DELIVERY SYSTEM

- Exhibit strong interaction with the mucin epithelial tissue
- Minimum impact on drug release.
- Good spreadability, wetting, swelling and solubility and biodegradability properties.
- Unaffected by the hydrodynamic conditions, food and pH changes.
- Easy to incorporate in various dosage forms.
- Show bioadhesive properties in both dry and liquid state.
- The Trans mucosa is relatively permeable with a rich blood supply, robust in comparison to the other mucosal tissues.
- Rapid adherence to mucosa.
- Bypass the first-pass effect.
- Easy access to the membrane sites so that the delivery system can be applied, localized and removed easily.[11-12]
- Improve the performance of many drugs, as they are having prolonged contact time with the mucosa.
- High patient acceptance compared to other non-oral routes of drug administration.
- Absorption of certain drugs across the Trans mucosa provides patients with a rapid onset of action, transmucosal drug delivery offers an alternative when enteral administration is impractical (e.g. in patients who have difficulty in swallowing, nausea or vomiting, or intestinal failure).[12]

LIMITATIONS

- Drugs which are unstable at buccal pH cannot be administered by this route.
- Only with small dose requirements can be administered.
- Drugs may be swallowed with saliva and lose the advantages of the buccal route. Only those drugs which are absorbed by passive diffusion can be administered by this route.
- Eating and drinking may be come restricted; however swallowing of the formulation by the patient may be possible.
- Over hydration may lead to the formation of a slippery surface and the structural integrity of the formulation get disrupted by the swelling and hydration of the bioadhesive polymers.[12]

RECENT ADVANCES IN ORAL DRUG DELIVERY SYSTEM[7, 11, and 12]

- Extensive efforts have recently been focused on targeting a drug or delivery system in a particular region of the oral cavity such as soft palate, for extended period of time, not only for local targeting of drugs but also for the better control of systemic drug delivery.
- Administration of vaccine antigens directly to various mucosal sites for the effective protection of mucosal surfaces against colonization and invasion of infectious agents have recently come into focus development of successful mucosal vaccines depends largely on the improvement of mucosal antigen delivery and on the discovery of new and effective mucosal adjuvant.
- Chitosan easily forms microparticles and nanoparticles which encapsulate large amounts of antigens such as ovalbumin, diphtheria toxoid or tetanus toxoid.
- It has been shown that ovalbumin-loaded chitosan microparticles are taken up by the Peyer's patches of the gut associated lymphoid tissue (GALT such studies can provide initial leads to suitable drug candidates for oral mucosal drug delivery. Recent works on such studies and their implication.
- On new opportunities for improving therapeutic modality.
- E.g. To achieve better bioavailability, rapid onset of action and convenient drug administration from oral transmucosal drug delivery been performed Various oral mucosal dosage forms that include toothpastes, mouthwashes, lozenges, gels, chewing gums, lollipops, films, patches, tablets and some other specialized devices. Most of them are patents and very few are available in market.
- It is increasingly apparent that successful progress in such investigations involves approach using diverse methodologies. For example, epithelial-mesenchymal interactions are likely to involve multiple mesenchymal factors acting in concert to establish and maintain epithelial form and, because of this complexity; the nature of the inductive influences is not likely to be elucidated in model systems unless individual variables can be rigidly controlled.

CONCLUSIONS

- The oral transmucosal drug delivery method has been found most suitable as compared with other systematic drug delivery systems. Nowadays, a significant development has been done in long-sustained delivery systems for systemic therapy. Oral transmucosal system allows a more rapid absorption into the blood stream as compared with oral administration to

the GIT and consequently offering an alternative means of drug administration, which is more comfortable.

On the basis of applications and advantages of oral transmucosal drug delivery method, it's concluded that the oro-trans mucosal route is a significant alternative for other drug delivery forms.

This concept can be used for optimizing the dose of drug and minimizing its undesirable effects. The buccal mucosa offers several advantages over controlled drug delivery for extended periods of time. The research on transmucosal drug delivery system is still in its early stage, and further advances need to be made for the successful translation of the concept into practical application in controlled drug delivery system (CDDS).

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