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REVIEW ARTICLE

Buccoadhesive Drug Delivery System: Need

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ABSTRACT

The present article focuses on the principles of mucoadhesive drug delivery systems based on adhesion to biological surfaces that are covered by mucus. Over the last few decade's pharmaceutical scientists throughout the world are trying to explore transdermal and transmucosal routes as an alternative to injections. Among the various transmucosal sites available, mucosa of the buccal cavity was found to be the most convenient and easily accessible site for the delivery of therapeutic agents for both local and systemic delivery as retentive dosage forms, because it has expanse of smooth muscle which is relatively immobile, abundant vascularization, rapid recovery time after exposure to stress and the near absence of langerhans cells. Direct access to the systemic circulation through the internal jugular vein bypasses drugs from the hepatic first pass metabolism leading to high bioavailability. This article reviews current status of various buccal bioadhesive dosage forms such as tablets, patches, hydrogels and films and describes the strategies to improve permeation of drugs through the Buccal mucosa.

Keywords: Bioavailability, First –pass metabolism, Buccoadhesive drug delivery system, Permeation.

INTRODUCTION

Mucoadhesive drug delivery systems are delivery system which utilized the property of bioadhesion of certain polymers which become adhesive on hydration and hence can be used for targeting a drug to a particular region of the body for extended periods of time[1]. The concept of mucoadhesion was introduced into controlled drug delivery in the early 1980s. The term 'bioadhesion' has been used to define as an interfacial phenomenon in which two materials, at least one of which is biological nature are held together by means of interfacial forces. The attachment could be between an artificial material and biological substrate, such as adhesion between a polymer and a biological membrane[2].

Mucoadhesive drug delivery systems prolong the residence time of the dosage form at the site of application or absorption. They facilitate an intimate contact of the dosage form with the underlying absorption surface and thus improve the therapeutic performance of the drug. In recent years, many such mucoadhesive drug delivery systems have been developed for oral, buccal, nasal, rectal and vaginal routes for both systemic and local effects. Buccal drug delivery has sever-al advantages over peroral delivery. Administration of compounds via the mucosa of the oral cavity avoids pre-systemic metabolism in the gastrointestinal (GI) tract and hepatic first pass elimination. In addition, the buccal mucosa is a well-vascularized tissue and is easily accessible for both application and removal of a delivery device. It's having facility to include permeation enhancer/enzyme inhibitor or pH-modifier in the formulation and versatility in designing as multidirectional or unidirectional release systems for local or systemic actions etc.

Drugs have been applied to the oral mucosa for topical applications for many years. However, recently there has been interest in exploiting the oral cavity as a portal for delivering drugs to the systemic circulation. Notwithstanding the relatively poor permeability characteristics of the epithelium, a number of advantages

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are offered by this route of administration. Foremost among these are the avoidance of first-pass metabolism, ease of access to the delivery site, and the opportunity of sustained drug delivery predominantly via the buccal tissues. Delivery can also be terminated relatively easily if required. The robustness of the epithelium necessary to withstand mastication also serves the drug delivery process well as fast cellular recovery follows local stress and damage[3].

The development of sustain release dosage form can achieve the aim of releasing the drug slowly for a long period but this is not sufficient to get sustained therapeutic effect. They may be cleared from the site of absorption before emptying the drug content. Instead, the mucoadhesive dosage form will serve both the purposes of sustain release and presence of dosage form at the site of absorption. In this regard, our review is high lighting few aspects of mucoadhesive drug delivery systems[4].

MUCOADHESIVE DRUG DELIVERY SYSTEM IN ORAL CAVITY[5]:

Drug delivery via the membranes of the oral cavity can be subdivided as follows:

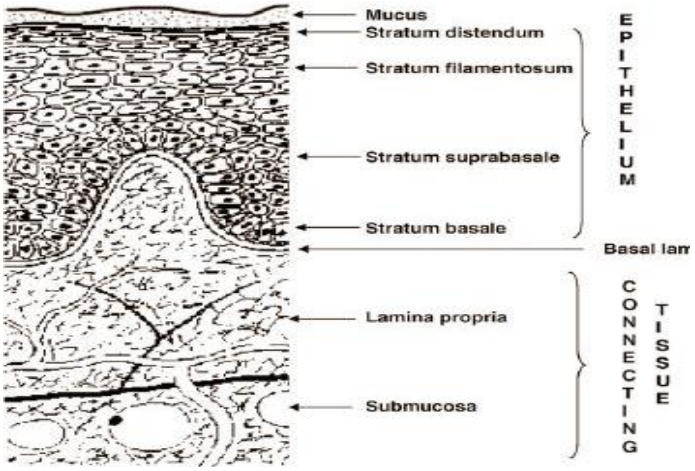
- **Sublingual delivery:** involves administration of drug via the sublingual mucosa to the systemic circulation.
- **Buccal delivery:** involves administration of drug via the buccal mucosa to the systemic circulation; and
- **Local delivery:** involves administration of bioadhesive system either to the palate, the gingiva or the cheek. These sites differ automatically on their parmeability of drugs, rate of drug delivery and ability to maintain drug delivery system for time required to release drug into the oral mucosa.

OVERVIEW OF BUCCAL MUCOSA:

Structure[6]

The oral mucosa is made up of an outermost layer of stratified squamous epithelium, which is covered with mucus and consists of stratum distendum, stratum filamentosum, stratum suprabasale, and a stratum basale. Below this layer lies a basal lamina, the lamina propria followed by the submucosa as the innermost layer. The epithelium serves as a mechanical barrier protecting the underlying tissues where as the lamina propria acts as a mechanical support and carries blood vessels and nerves. The stratified squamous epithelium has a mitotically active basal layer and produces different cell layers, where cells are shed from the Surface of the epithelium. The epithelium 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 differentiate from the basal layers to the superficial layers. The turnover time for the oral mucosal epithelium has been estimated at 5-6 days. The oral mucosal thickness varies depending on the site: the buccal mucosa measures at 500-800 ìm, while the mucosal thickness of the hard and soft palates, the floor of the mouth, the ventral tongue, and the gingival measure at about 100-200 ìm. The mucosa of the soft palate, the sublingual, and the buccal are the non-keratinized regions of oral mucosa. These are more permeable than keratinized regions such as that of hard palate due to the composition of intercellular lipids comprising those particular regions. The keratinized epithelia contain predominantly the neutral lipids like ceramides and acylceramides which have been associated with the barrier function. These epithelia are relatively impermeable to water. The non-keratinized epithelia are composed of small amounts of neutral but polar lipids, mainly cholesterol sulfate and glucosyl ceramides. These epithelia have been found to be considerably more permeable to water than keratinized epithelia. Structure of oral mucosa consist of numerous racemose, mucous or serous glands are present in the sub mucous tissue of the cheeks.

Figure No.1[6] Section of Buccal mucosa:



WHY BUCCAL MUCOSA? [6]

The oral mucosa is highly perfused with blood vessels with a high blood flow rate of 20-30mL/min for each 100gm of the tissue. The blood vessels are close to the surface and the lymphatic drainage is also well developed. Hence therapeutic concentrations of the drug can be achieved rapidly. 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. The permeability coefficients for most compounds are consistently higher for the buccal and oral mucosa than for normal and hydrated skin.

PERMIABILITY[7, 8]:

The permeability barrier property of the oral mucosa is predominantly due to intercellular materials derived from the so-called "membrane coating granules" (MCGs). MCGs are spherical or oval organelles that are 100–300 nm in diameter and found in both keratinized and non keratinized epithelia. These organelles have also been referred to as 'small spherically shaped granules', 'corpusula', 'small dense granules', 'small lamellated bodies', 'lamellated dense bodies', 'keratinosomes', 'transitory dense bodies', and 'cementsomes'[7]. MCGs start forming and at the apical 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. This barrier exists in the outermost 200µm of the superficial layer. Permeation studies have been performed using a number of very large molecular weight tracers, such as horseradish peroxidase and lanthanum nitrate. In both keratinized and non-keratinized epithelia, the limit of penetration coincided with the level where the MCGs could be seen adjacent to the superficial plasma membranes of the epithelial cells. Since the same result was obtained in both keratinized and non-keratinized epithelia, keratinization by itself is not expected to play a significant role in the barrier function. The components of the MCGs in keratinized and non-keratinized epithelia are different, however. The MCGs of keratinized epithelium are composed of lamellar lipid stacks, whereas the non-keratinized epithelium contains MCGs that are non-lamellar. The MCG lipids of keratinized epithelia include sphingomyelin, glucosylceramides, ceramides, and other nonpolar lipids, however for non-keratinized epithelia, the major MCG lipid components are cholesterol esters, cholesterol, and glycosphingolipids. The structure of the basement membrane is not dense enough to exclude even relatively large molecules.

ENVIRONMENT[9] :

The oral cavity is marked by the presence of saliva produced by the salivary glands and mucus which is secreted by the major and minor salivary glands as part of saliva.

Role of Saliva:

- Protective fluid for all tissues of the oral cavity.
- Continuous mineralization / demineralization of the tooth enamel.
- To hydrate oral mucosal dosage forms.

Role of Mucus:

- Made up of proteins and carbohydrates.
- Cell-cell adhesion
- Lubrication
- Bioadhesion of mucoadhesive drug delivery systems.

Oral cavity membrane	Thickness (mm)	Surface area (cm^2)
Buccal mucosa	500-600	5.2
Sublingual mucosa	100-200	26.5
Gingival mucosa	200	--
Palatal	250	20.1

Table no 1[9]: Thickness and surface area of oral cavity membranes:

NEED OF MUCOADHESIVE DRUG DELIVARY SYSTEM[10] :

- Control release.
- Target and localized drug delivery.
- By pass first pass metabolism.
- Avoidance of drug degradation.
- Prolonged effect.
- High drug flux through absorbing tissues.
- Reduction in fluctuation in steady state plasma level.

ADVANTAGES[11-14]:

- Buccal mucosa has rich blood supply due to it's high vascularization and so the drug easily absorbed through it.
- Prolongs the residence time of the dosage form at the site of absorption.
- Faster onset of action is achive due to the mucosal surface.
- the drug gain direct entry into the systemic circulation thereby bypassing the first pass effect.
- avoidance of presystemic elimination within the gastrointestinal tract.
- good accesability and it has better patient complience due to the elimination of associated pain with injection.
- Large contact of the sarface of the oral cavity contributes to rapid and extensive drug absorption.
- nausea and vomitting are greatly avoided.

Disadvantages[11-14]:

- Drugs which are unstable at buccal pH cannot be administered.
- Drugs which irritate the mucosa or have a bitter or unpleasant taste or an obnoxious odor cannot be administered by this route.
- Only drug with small dose requirement can be administered.
- Only those drugs which are absorbed by passive diffusion can be administered by this route.
- Eating and drinking may become restricted.
- There is an ever present possibility of the patient swallowing the dosage form.
- Over hydration may leads to slippery surface and structural integrity of the formulation may get

disrupted by this swelling and hydration of the bioadhesive polymers.

- Drugs contained in the swallowed saliva follows the pre-oral and advantages of buccal route are lost.

ROUTES OF DRUG ABSORPTION[15]:

The are two permeation pathways for passive drug transport across the oral mucosa :

- Paracellular routes
- Transcellular routes.

Permeants can use these two routes simultaneously, but one route is usually preferred over the other depending on the physicochemical properties of the diffusant. Since the intercellular spaces and cytoplasm are hydrophilic in character, lipophilic compounds would have low solubilities in this environment. The cell membrane, however, is rather lipophilic in nature and hydrophilic solutes will have difficulty permeating through the cell membrane due to a squat partition coefficient. Therefore, the intercellular spaces pose as the main barrier to permeation of lipophilic compounds and the cell membrane acts as the major transport barrier for hydrophilic compounds. Since the oral epithelium is stratified, solute permeation may involve a combination of these two routes. The route that predominates, however, is generally the one that provides the least amount of hindrance to passage.

MECHANISM OF BIOADHESION[16]:

Bioadhesion is an interfacial phenomenon in which two materials, at least one of which is biological, are held together by means of interfacial forces. The attachment could be between an artificial material and biological substrate, such as adhesion between polymer and/or copolymer and a biological membrane. In case of polymer attached to the mucin layer of the mucosal tissue, the term “mucoadhesion” is employed. “Bioadhesive” is defined as a substance that is capable of interacting with biological material and being retained on them or holding them together for extended period of time.

In the study of adhesion generally, two steps in the adhesive process have been identified, which have been adapted to describe the interaction between mucoadhesive materials and a mucous membrane.

Type 1. Contact Stage

An intimate wetting occurs between the mucoadhesive and mucous membrane. In some cases these two surfaces can be mechanically brought together, e.g. placing and holding a delivery system within the oral cavity, eye or vagina.

Type 2. Consolidation Stage

Different physicochemical interactions happen to combine and toughen the adhesive joint, leading to long-lasting adhesion**.** Mucoadhesive materials adhere most strongly to solid dry surfaces as long as they are activated by the presence of moisture and will effectively plasticize the system allowing mucoadhesive molecules to become free, conform to the shape of the surface and bond predominantly by hydrogen and weaker van der Waal bonding.

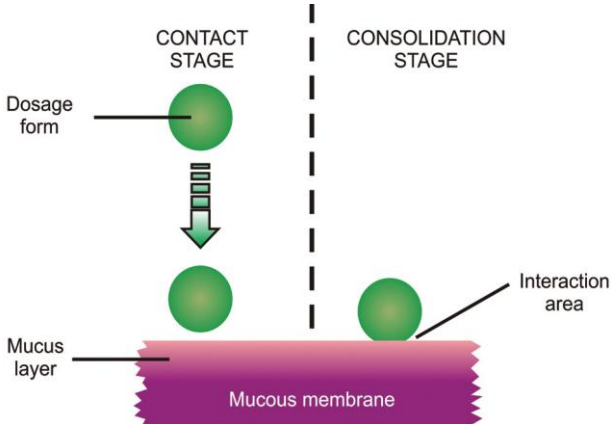


Figure no 2: The two steps of the mucoadhesion process.

Type 3. The Removal Mechanism

Adhesive failure will normally occur at the weakest component of the joint. For weaker adhesives this would be the mucoadhesive-mucus interface, for stronger adhesives this would initially be the mucus layer, but later may be the hydrating mucoadhesive material.

THEORIES OF MUCOADHESION:

- **Adsorption theory[16]:** According to this theory, after an initial contact between two surfaces, the materials adhere because of surface forces acting between the atoms in the two surfaces. Two types of chemical bonds such as primary covalent (permanent) and secondary chemical bonds (including electrostatic forces, vander Waals forces and hydrogen and hydrophobic bonds) are involved in the adsorption process.
- **Electronic theory[16]:** According to this theory, electronic transfer occurs upon contact of an adhesive polymer and the mucus glycoprotein network because of differences in their electronic structure. This result in the formulation of an electronic double layer at the interface adhesion occurs due to attractive forces across the double layer.
- **Diffusion Theory[18]:** Interpenetration of the chains of polymer and mucus may lead to formation of a sufficiently deep layer of chains. The diffusion mechanism is the intimate contact of two polymers or two pieces of the same polymer. During chain interpenetration the molecules of the polymer and the dangling chains of the

glycoproteinic network are brought in intimate contact. Due to the concentration gradient, the bioadhesive polymer chains penetrate at rates that are dependent on the diffusion coefficient of a macromolecule through a cross-linked network and the chemical potential gradient. In addition, good solubility of the bioadhesive medium in the mucus is required in order to achieve bioadhesion. Thus the difference of the solubility parameters of the bioadhesive medium and the glycoprotein should be as close to zero as possible. Thus the bioadhesive medium must be of similar chemical structure to the glycoproteins.

- **Wetting theory[19]:** postulates that if the contact angle of liquids on the substrate surface is lower, then there is a greater affinity for the liquid to the substrate surface.
- **Fracture theory[19]:** Fracture theory of adhesion is related to separation of two surfaces after adhesion. The fracture strength is equivalent to adhesive strength.

Factors affecting muco/ bioadhesion[20]:

Structural and physicochemical properties of a potential bioadhesion material influence bioadhesion.

Polymer related factors:

- **Molecular weight :**
  The bioadhesive force increases with molecular weight of polymer, up to 1, 0000 and beyond this level there is no much effect. To allow chain interpenetration, the polymer molecule must have an adequate length.
- **Concentration of active polymers :**
  There is an optimum concentration of polymer corresponding to the best bioadhesion infect, in concentrated solutions, the coiled molecules become solvent poor and the chains available for interpenetration are not numerous, for solid dosage forms such as tablets showed that the higher the polymer concentration the stronger the bioadhesion.
- **Flexibility of polymer chain:**
  Flexibility is an important factor for interpenetration and enlargement. As watersoluble polymers become cross linked, the mobility of individual polymer chain decreases. As the cross linking density increases, the effective length of the chain which can penetrate into the mucous layer decreases further and mucoadhesive strength is reduced.

Environment related factors:

- **pH:**
  pH influences the charge on the surface of both mucus and the polymers. Mucus will have a different charge density depending on pH because of difference in dissociation of functional groups on the carbohydrate moiety and amino acids of the polypeptide back bone.
- **Applied strength:**
  To place a solid bioadhesive system, it is necessary to apply a defined strength.
- **Initial contact time:**
  The mucoadhesive strength increases as the initial contact time increases.
- **Selection of the model substrate surface:**
  The viability of biological substrate should be confirmed by examining properties such as permeability, electrophysiology of histology.
- **Swelling:**
  Swelling depends on both polymers concentration and on presence of water. When swelling is too great a decrease in bioadhesion occurs.

Physiological Variables[21]:

- **Mucin turnover:** The natural turnover from the mucus layers is important for at least two reasons. The mucin turnover is expected to limit the residence time of the mucoadhesive on the mucus layers.
  Mucin turnover results in substantial amounts of soluble mucin molecules.
- **Diseased states:** Physicochemical properties of mucus are known to change during diseased states, such as common cold, gastric ulcers, ulcerative colitis, cystic fibrosis, bacterial and fungal infections of the female reproductive tract and inflammatory conditions of the eye.

STRUCTURE AND DESIGN OF BUCCAL DOSAGE FORM[22]:

Buccal Dosage form can be of two types:

- **Matrix type:** The buccal dosage form designed in a matrix configuration contains drug, adhesive and additives mixed together. Transmucosal drug delivery systems can be bidirectional or unidirectional. Bi-directional dosage form release drug in both the mucosa and the mouth**.**
- **Reservoir type:** The buccal dosage form 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 dosage form deformation and disintegration while in the mouth; and to prevent drug loss.

Additionally, the dosage form can be constructed to undergo minimal degradation in the mouth, or can be designed to dissolve almost immediately. Unidirectional dosage form release the drug only into the mucosa.

Investigations on the buccal drug delivery systems[23]:

Several buccal adhesive delivery devices were developed at the laboratory scale by many researchers either for local or systemic actions. They are broadly classified in to,

- Solid buccal adhesive dosage forms
- Semi-solid buccal adhesive dosage forms
- Liquid buccal adhesive dosage forms

Solid buccal adhesive formulations

Dry formulations achieve bioadhesion via dehydration of the local mucosal surface.

Tablets: Several bioadhesive tablet formulations were developed in recent years either for local or systemic drug delivery. Tablets that are placed directly onto the mucosal surface have been demonstrated to be excellent bioadhesive formulations. However, size is a limitation for tablets due to the requirement for the dosage form to have intimate contact with the mucosal surface. These tablets adhere to the buccal mucosa in presence of saliva. They are designed to release the drug either unidirectionally targeting buccal mucosa or mutidirectionally
in to the saliva.

Microparticles: Bioadhesive microparticles offer the same advantages as tablets but their physical properties enable them to make intimate contact with a lager mucosal surface area. In addition, they can also be delivered to less accessible sites including the GI tract and upper nasal cavity. The small size of microparticles compared with tablets means that they are less likely to cause local irritation at the site of adhesion and the uncomfortable sensation of a foreign object within the oral cavity is reduced.

Wafers: The delivery system is a composite wafer with surface layers possessing adhesive properties, while the bulk layer consists of antimicrobial agents, biodegradable polymers and matrix polymers.

Lozenges: Bioadhesive lozenges may be used for the delivery of drugs that act topically within the mouth including antimicrobials, corticosteroids, local anesthetics, antibiotics and antifungals. Conventional lozenges produce a high initial release of drug in the oral cavity, which rapidly declines to subtherapeutic levels, thus multiple daily dosing is required. A slow release bioadhesive lozenge offers the potential for prolonged drug release with improved patient compliance. Codd and Deasy investigated bioadhesive lozenges as a means to deliver antifungal agents to the oral cavity.

Semi-solid dosage forms

Gels: Gel forming bioadhesive polymers include crosslinked polyacrylic acid that has been used to adhere to mucosal surfaces for extended periods of time and provide controlled releaseof drugs. Gels have been widely used in the delivery of drugs to the oral cavity. Advantages of gel formulations include their ability to form intimate contact with the mucosal membrane and their rapid release of drug at the absorption site. A limitation of gel formulations lies on their inability to deliver a measured dose of drug to the site. They are therefore of limited use for drugs with narrow therapeutic window.

	Bioadhesive polymer used
Buprenorphine	HEMA and Polymeg
Buspirone HCL	Carbopol 974, HPMCK4M
Chlorhexidine diacetate	Chitosan and sodium alginate
Chlorpheneramine maleate	Hakea gum, Carbopol 934, HPMC
Clotrimazole	Carbopol 974P, HPMC K4M
Carvedilol	Carbopol 974P, HPMC K4M
Carbamazepine	HPMC and Carbopol
Diltiazem HCl	Carbopol 934, HPMCK4M
Ergotamine tartrate	Carboxyvinyl polymer and HPC
Felodipine	HP-β-CD - felodipine complex and HPMC
Hydralazine HCL	Carbopol 934P and CMC
Metaclopromide	Carbopol, HPMC, PC, Sodium CMC
Metronidazole	HEC, HPC, HPMC, or Na CMC combined with Carbopol 940,
Miconazole nitrate	HPMC, sodiumCMC, Carbopol, sodium Alginate
Nifedipine	CMC and Carbopol
Pindolol	Carbopol 934 and sodium CMC; HPMC and HPC
Propranolol HCl	HPMC and PC
Piroxicam	HPMC and Carbopol 940
Omeprazole	Sodium alginate, HPMC
Ketoprofen	Chitosan and sodium Alginate
Verapamil	HPC-M, CP 934
Triamcilone	HPC, CP-934
Hydrocortisone Acetate	HPMC (methocelk4m), carbapol934P,
Pentazocine	CP-934P, HPMC

Table no 2: List of the drugs investigated for buccal mucoadhesive tablets[24]

Patches/films: Flexible films may be used to deliver drugs directly to a mucosalmembrane. They also offer advantages over creams and ointments in that they provide a measured dose of drug to the site. Buccal adhesive films are already in use commercially for example, Zilactin used for the therapy of canker sores, cold sores and lip sores.

Liquid dosage forms: Viscous liquids may be used to coat buccal surface either as protectants or as drug vehicles for delivery to themucosal surface. Traditionally, pharmaceutically acceptable polymerswere used to enhance the viscosity of products to aid their retention in the oral cavity. Dry mouth is treated with artificial saliva solutions that are retained on mucosal surfaces to provide lubrication. These solutions contain sodium CMC as bioadhesive polymer.

Delivery of proteins and peptides : The buccal mucosa represents a potentially important site for controlled delivery of macromolecular therapeutic agents, such as peptides and protein drugs with some unique advantages such as the avoidance of hepatic first-pass metabolism, acidity and protease activity encountered in the gastrointestinal tract.

Toxicity and irritancy associated with buccal drug delivery[25,26] :

Formulations that produce local damage at the site of application, such as ulceration of the mucosa, would preclude their widespread usage as a result of the associated pain and discomfort. This is particularly important in buccal drug delivery where the formulation is in contact with the mucosa for extended periods. Toxic effects can arise from the drug itself, the bioadhesive or from other components of the formulation. For example, carbomers have been reported to produce mucosal irritation believed to result from a localised low pH, whereas lectins have been shown to be cytotoxic. Excipients such as absorption enhancers (e.g., sodium dodecyl sulfate) have also been reported to be irritant.

Future prospect[27, 28] :

The main impediment to the use of many hydrophilic macromolecular drugs as potential therapeutic agents is their inadequate and erratic oral absorption. The future challenge of pharmaceutical scientists will not only be polypeptide cloning and synthesis, but also to develop effective non-parenteral delivery of intact proteins and peptides to the systemic circulation. Buccal permeation can be improved by using various classes of transmucosal and transdermal penetration enhancers such as bile salts, surfactants, fatty acids and derivatives, chelators and cyclodextrins.

Researchers are now looking beyond traditional polymer networks to find other innovative drug transport systems. Much of the development of novel materials in controlled release buccal adhesive drug delivery is focusing on the preparation and use of responsive polymeric system using copolymer with desirable hydrophilic/hydrophobic interaction, block or graft copolymers, complexation networks responding via hydrogen or ionic bonding and new biodegradable polymers especially from natural edible sources. At the current global scenario, scientists are finding ways to develop buccal adhesive systems through various approaches to improve the bioavailability of orally less/inefficient drugs by manipulating the formulation strategies like inclusion of pH modifiers, enzyme inhibitors, permeation enhances etc. Novel buccal adhesive delivery system, where the drug delivery is directed towards buccal mucosa by protecting the local environment is also gaining interest. Currently solid dosage forms, liquids and gels applied to oral cavity are commercially successful. Thus,increasing the absorption rate and minimizing the metabolism at the site of drug delivary are the major stumbling blocks in the administration of peptide drug through the oral mucosa.as a result of formulating scintists continue to seek improved delivery system via mucosal route.

CONCLUSION:

Mucoadhesive systems prolongs the residence time of the dosage form at the site of application or absorption and facilitates an intimate contact of the dosage form with the underline absorption surface and thus contributes to improved and/or better therapeutic performance of the drug. It is the developing area whose goal is the development of new devices and more “intelligent” polymers,with the great influx of new molecules elucidate from drug research. mucoadhesive systems may play an increasing role in the development of new pharmaceuticals. For safe and effective buccal permeation, absorption enhancer is a crucial component for a prospective future in the area of buccal drug delivery.

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