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Critical review on Buccal Mucoadhesive Drug Delivery System

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ABSTRACT

Buccal mucosa is the preferred site for both systemic and local drug action. The mucosa has a rich blood supply and it relatively permeable. Mucoadhesion can be defined as a state in which two components, of which one is of biological origin, are held together for extended periods of time by the help of interfacial forces. Mucoadhesion is a complex phenomenon which involves wetting, adsorption and interpenetration of polymer chains. Buccal mucoadhesive systems remain in close contact with the absorption tissue, the mucous membrane releasing the drug at the action site leading to increase in bioavailability (both local and systemic effects). Extending the residence time of a dosage form at a particular site and controlling the release of drug from the dosage form are useful especially for achieving controlled plasma level of the drug as well as improving bioavailability. In the present review article discusses with the buccal membrane, theory and kinetics behind buccal mucoadhesion, different types of buccal formulation advantages and disadvantages of buccal mucoadhesive drug delivery system.

Keywords: Buccal mucosa, permeable, biological origin, bioavailability.

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INTRODUCTION

The buccal region of the oral cavity is an attractive target for administration of the drug of choice. Buccal delivery involves the administration of the desired drug through the buccal mucosal membrane lining of the oral cavity. Because after oral administration many drugs show first-pass metabolism, which leads to a lack significant correlation between membrane permeability, absorption, and bioavailability[1]. The oral administrations of many drugs show first-pass metabolism which results in to lower bioavailability. Limitation associated with parenteral delivery and poor oral bioavailability needs alternative route for delivery of such drugs. The alternative route such as pulmonary, ocular, nasal, rectal, buccal, sublingual, vaginal, and transdermal are available for study. Among the various routes transmucosal routes, the mucosal lining of the oral cavity offers some distinct advantages[2]. Oral cavity is richly vascularized and more accessible for the administration and dose termination. High bioavailability is achieved due to direct access to the systemic circulation through the internal jugular vein bypass drugs from the hepatic first pass metabolism. Buccal drug delivery has a high patient compliance compared to other non-oral routes of drug administration. The limitations associated are the low permeability of the buccal membrane, specifically when compared to the sublingual membrane, and a smaller surface area. The surface area available for drug absorption is 170 cm^2, of which ~50 cm^2 in oral cavity represents non-keratinized tissues, including the buccal membrane. Secretion of saliva leads to further dilution of the drug also swallowing of saliva can also potentially lead to the loss of drug and, ultimately removal of the dosage form. These are some of the limitations that are associated with buccal drug delivery[3]. Various approaches of buccal drug delivery system are being explore to avoid inconvenience caused due to choking of drug delivery system due to involuntary swallowing by the patient also patients are having limitations during and eating when the drug delivery system is administered.

The delivery of drug into oral mucosal cavity is classified into three categories[4]:-

- Sublingual delivery- which is systemic delivery of drug through the mucosal membranes lining the floor of the mouth.
- Buccal delivery- which is drug administration through the mucosal membranes lining the cheeks.
- Local delivery- which is drug delivery into the oral cavity.

Overview of the oral mucosa Structure[5-7]:

The oral cavity is lined with mucous membranes with a total surface area of 100 cm^2. It is

possible to observe several distinct areas: the floor of mouth (sublingual), the buccal mucosa (cheeks), the gums (gingival), the palatal mucosa and the lining of the lips. 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.

Drug can follow transcellular or Paracellular route. In Transcellular route drug cross the cell membrane and entering the cell and in Paracellular dug passing between the cells. Drug molecule may transfer by transcellular or Paracellular route, but depending upon the physicochemical properties of the diffusant one route usually is more effective and the drug molecule will follow the path for easy diffusion. As the intercellular spaces are less lipophilic in character than the cell membrane, hydrophilic compounds have higher solubility in this environment. The cell membrane, however, is highly lipophilic in nature, and hydrophilic solutes have great difficulty permeating the cell membrane because of a low partition coefficient. Therefore, the intercellular spaces pose the major barrier to passive permeation of lipophilic compounds, and the cell membrane acts as the major transport barrier for hydrophilic compounds. Because 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[8].

Barriers to penetration across buccal mucosa

Basement membrane[9-12]:

Superficial layers of the oral epithelium represent the primary barrier for drug molecule for entry; from literature survey it is evident that the basement membrane is also responsible for limiting the passage of drug molecule across the junction between epithelium and connective tissue. A similar mechanism appears to operate in the opposite direction. The charge on the constituents of the basal lamina may limit the rate of penetration of lipophilic compounds that can traverse the superficial epithelial barrier relatively easily.

Mucus:

The epithelial cells of buccal mucosa are surrounded by the intercellular ground substance called mucus with the thickness varies from 40 μm to 300 μm**5**. Mucus is composed chiefly of mucins and inorganic salts suspended in water. Mucins are a family of large, heavily glycosylated

proteins composed of oligosaccharide chains attached to a protein core. Three quarters of the protein core are heavily glycosylated and impart a gel like characteristic tomucus. Mucins contain approximately 70–80% carbohydrate, 12–25% protein and up to 5% ester sulphate. The dense sugar coating of mucins gives them considerable water-holding capacity and also makes them resistant to proteolysis, which may be important in maintaining mucosal barriers.

Saliva: The mucosal surface has a salivary coating estimated to be 70 μm thick, which act as unstirred layer. Within the saliva there is a high molecular weight mucin named MG1 that can bind to the surface of the oral mucosa so as to maintain hydration, provide lubrication, concentrate protective molecules such as secretory immunoglobulins, and limit the attachment of microorganisms. Several independent lines of evidence suggest that saliva and salivary mucin contribute to the barrier properties of oral mucosa. A constant flowing down of saliva within the oral cavity makes it very difficult for drugs to be retained for a significant amount of time in order to facilitate absorption in this site.

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.

MECHANISM OF MUCOADHESION

As stated, mucoadhesion is the attachment of the drug along with a suitable carrier to the mucous membrane. Mucoadhesion is a complex phenomenon which involves wetting, adsorption and interpenetration of polymer chains. Mucoadhesion has the following mechanism

1. Intimate contact between a bioadhesive and a membrane (wetting or swelling phenomenon)
2. Penetration of the bioadhesive into the tissue or into the surface of the mucous membrane(interpenetration).

Residence time for most mucosal routes is less than an hour and typically in minutes, it can be increased by the addition of an adhesive agent in the delivery system which is useful to localize the delivery system and increases the contact time at the site of absorption. The exact mechanism of mucoadhesion is not known but an accepted theory states that a close contact between the mucoadhesive polymer and mucin occurs which is followed by the interpenetration of polymer and mucin. The adhesion is prolonged due to the formation of van der vaals forces, hydrogen bonds and electrostatic bonds[13-14].

THEORIES OF MUCOADHESION[15-17]:

Wettability theory:

The ability of bioadhesive or mucus to spread and develop intimate contact with its corresponding substrate is an important factor in bond formation. The wetting theory, was developed predominantly in regard to liquid adhesives, uses interfacial tensions to predict spreading and in turn adhesion.5-7 The study of surface energy of polymers and tissues to predict mucoadhesive performance has been given considerable attention.8-11 The contact angle(Q) which should ideally be zero for adequate spreading is related to interfacial tensions(g) as per the Young's equation,

$$g_{tg} = g_{bt} + g_{bg} \cos Q$$

Where the subscripts t,g and b represent tissue, gastrointestinal contents and bioadhesive polymer respectively, for spontaneous wetting to occur.

$$gtb \geq gbt + gbg$$

The spreading coefficient, Sb/t can be given by,

$$Sb/t = g_{tg} - g_{bt} - g_{bg}$$

For the bioadhesion to take place the spreading coefficient must be positive, hence it is advantageous to maximize the interfacial tension at the tissue-GI contents interface and minimizing the surface tension at the other two interfaces. The interfacial tension can be measured by methods like the Wilhelmy plate method. It has been shown that the BGtissue interfacial tension can be calculated as,

$$g_{bt} = g_b + g_t - 2F(gbgt)1/2$$

Where the values of F(interaction parameter) can be found in published papers thus by the wetting theory it is possible to calculate spreading coefficients for various bioadhesives over biological tissues and predict the intensity of the bioadhesive bond.

Electronic theory:

The electronic theory depends on the assumption that the bioadhesive material and the target biological material have different electronic surface characteristics. Based on this, when two surfaces come in contact with each other, electron transfer occurs in an attempt to balance the Fermi levels, resulting in the formation of a double layer of electrical charge at the interface of the bioadhesive and the biologic surface. The bioadhesive force is believed to be present due to the attractive forces across this double layer.

Fracture theory:

This is by-far the most accepted theory on bioadhesion. It explains the forces required to separate the two surfaces after adhesion has taken place. It measures the maximum Tensile stress(sm) produced during detachment as follows.

$$s_m = F_m/A_o$$

Where Fm and Ao represent the maximum force of detachment and the total surface area Respectively. In a uniform single-component system, fracture strength(sf), which is equal to the maximum stress of detachment(sm), is proportional to the fracture energy(gc), Youngs modulus of elasticity(E) and the critical crack length(c) of the fracture site as follows,20

$$s_f \_ (gcE/c)^{1/2}$$

fracture energy can be obtained by the sum of the reversible work of adhesion, Wr(work done to produce new fracture surfaces) and the irreversible work of adhesion, Wi(work of plastic deformation),

$$g_c = W_r + W_i$$

Adsorption theory:

This theory states that the bioadhesive bond formed between an adhesive substrate and the tissue is due to the weak van der waals forces and hydrogen bond formation. It is one of the most widely accepted theories of bioadhesion.

Diffusion theory:

The concept of the interpenetration and entanglement ob the bioadhesive polymer chains and mucous polymer chains is supported by the diffusion theory. The bond strength increases with the increase in the degree of the penetration. This penetration is dependent on the concentration gradients and the diffusion coefficients. It is believed that interpenetration in the range of 0.2-0.5Bm is required to produce effective bond strength. The penetration depth (l) can be estimated by

$$l = (tD_b)^{1/2}$$

Where t is the time of contact and Db is the diffusion coefficient of the bio adhesive material in the mucus.

ADVANTAGES OF MUCOADHESIVES

A prolonged residence time at the site of drug action or absorption. A localization of drug action of the delivery system at a given target site. An increase in the drug concentration gradient due to the intense contact of particles with the mucosal. A direct contact with intestinal cells that is

the first step before particle absorption. Ease of administration. Termination of therapy is easy (except gastrointestinal) Permits localization of drug to the oral cavity for a prolonged period of time. Can be administered to unconscious patients except gastrointestinal offers an excellent route, for the systemic delivery of drugs with high first pass metabolism, thereby offering a greater bioavailability[18].

A significant reduction in dose can be achieved there by reducing dose related side effects.

Drugs which are unstable in the acidic environment are destroyed by enzymatic or alkaline environment of intestine can be administered by this route Eg Buccal sublingual, vaginal. Drugs which show poor bioavailability via the oral route can be administered conveniently it offers a passive system of drug absorption and does not require any activation. The presence of saliva ensures relatively large amount of water for drug dissolution unlike in case of rectal and transdermal routes Systemic absorption is rapid (SGanga,2007; GCRajput etal,2010) This route provides an alternative for the administration of various hormones, narcotic analgesic, steroids, enzymes, cardiovascular agents etc. The buccal mucosa is highly perfused with blood vessels and offers a greater permeability than the skin .Less dosing frequency Shorter treatment period Increased safety margin of high potency drugs due to better control of plasma levels Maximum utilization of drug enabling reduction in total amount of drug administered Improved patient convenience and compliance due to less frequent drug administration. Reduction in fluctuation in steady state levels and therefore better control of disease condition and reduced intensity of local or systemic side effects[19].

Limitations[20]

Drug administration via the buccal mucosa has certain limitations

Drugs, which irritate the oral mucosa, have a bitter or unpleasant taste, odour, cannot be administered by this route.

Drugs, which are unstable at buccal pH cannot be administered by this route.

Only drugs with small dose requirements can be administered.

Drugs may swallow with saliva and loses the advantages of buccal route.

Only those drugs, which are absorbed by passive diffusion, can be administered by this route.

Eating and drinking may become restricted.

Swallowing of the formulation by the patient may be possible.

Over hydration may lead to the formation of slippery surface and structural integrity of the formulation may get disrupted by the swelling and hydration of the bioadhesive polymers.

Buccal adhesive polymers[21]

A polymer is a molecule made up of a chain of repeating units which are chemically bonded together. Adhesives are substances which are used to glue things together. A polymer adhesive is a synthetic bonding substance made from polymers and is considered to be stronger, more flexible and have greater impact resistance than other forms of adhesives. The term is derived from the Greek words: polys meaning many, and meros meaning parts. Bioadhesive polymers should possess certain physicochemical features including hydrophilicity, numerous hydrogen bond-forming groups, flexibility for interpenetration with mucus and epithelial tissue, and visco-elastic properties

Ideal characteristics[22]

1. Polymer and its degradation products should be non-toxic, non-irritant and free from leachable impurities.
2. Polymer should have good wetting property, solubility characteristics, and biodegradability properties.
3. Quick adhesion property and should have sufficient mechanical strength.
4. Should possess peel, tensile and shear strengths at the bioadhesive range.
5. Polymer must be easily available and its cost should not be high.
6. Should show bioadhesive properties in both dry and liquid state.
7. Should demonstrate local enzyme inhibition and penetration enhancement properties.
8. Should demonstrate acceptable shelf life.
9. Should have optimum molecular weight.
10. Should possess adhesively active groups.
11. Should have required spatial conformation.
12. Should be sufficiently cross-linked but not to the degree of suppression of bond forming groups.
13. Should not aid in development of secondary infections such as dental caries.

Different bioadhesive dosages form:[12]**-**

Buccal chewing gum:-

Some commercial products of buccal chewing gum are available in the market **15** like Caffeine chewing gum, Stay Alert, was developed recently for alleviation of sleepiness. It is absorbed at a significantly faster rate and its bioavailability was comparable to that in capsule formulation. Nicotine chewing gums (e.g., Nicorette and Nicotinell) have been marketed for smoking cessation. The permeability of nicotine across the buccal mucosa is faster than across the skin.

Bioadhesive hydrogel tablets:-

Bioadhesive hydrogel tablets are similar to conventional tablets and the bioadhesive tablet easily can adhere to the buccal mucosa and are prepared by wet granulation, dry granulation, or direct compression processes. Drug is released upon the hydration and adhesion of the device. Buccal tablets should be fabricated and optimized for swelling behavior and drug release to ensure a prolonged period of bioadhesion and sustained or controlled release. Generally, the tablets are formulated with flat punches with dimensions less than 10 mm in diameter and 2 mm thick to aid in establishing intimate contact with buccal mucosa and reduce their interference with normal activities. The excipients which is used for preparation of bioadhesive tablets are water soluble such as high molecular weight polyethylene glycols and manitol because the tablets contain some mucoadhesive component.A single-layer buccal tablet of triamcinolone acetonide, Aftac, is used in the treatment of aphthous ulcers.

Bilayer buccoadhesive tablets:-

Specialized tablet formulations with two layers buccoadhesive tablets are being designed to achive biphasic drug release and minimize drug leakage into buccal cavity, Iga and Ogawa formulated a slowly disintegrating gingival tablet for sustained release of isosorbide dinitrate and nitroglycerin. Flatfaced tablets 8 mm in diameter were prepared using lactose and hydroxypropyl cellulose. In order to control the deformation of the tablet caused by softening and mouth movements, they were covered with a bioadhesive containing polyethylene film with a 5 mm hole in the center of the top surface. When evaluated in dogs, these tablets remained in position for about 10 hours, whereas plain tablets disintegrated within 3–6 hours. Constant blood drug levels were maintained for about 10 hours from covered tablets. It has been shown that the rate of tablet disintegration, which in turn refers the buccal residence and the drug blood levels, can be controlled by changing the size of hole. A size larger than 50% of the top surface of tablets is suggested to obtain a constant disintegration rate.

Biobadhesive Spray:

Buccoadhesive sprays are gaining important over other dosage forms because of flexibility, comfort, high surface area and availability of drug in solution form.The first FDA-approved (1996) formulation was developed by fentanyl Oralet ™ to take advantage of oral transmucosal absorption for the painless administration of an opioid in a formulation acceptable to children. In 2002, the FDA approved Subutex (buprenorphine) for initiating treatment of opioid dependence (addiction to opioid drugs, including heroin and opioid analgesics) and Suboxone (buprenorphine

and naloxone) for continuing treatment of addicts. In 2005, Oral-lyn buccal spray was approved for commercial marketing and sales in Ecuador .

Thiolated tablet:

Thiolated tablet formulated with thiolated polymers which is also called as a thiomers.These are hydrophilic macromolecules exhibiting free thiol groups on the polymeric back bone. These polymers are capable to forming disulphide bonds with cystine rich subdomains of mucous glycoprotein covering mucosal membrane. The bridging structure is most commonly used in biological systems to utilize the binding of drug on the mucosal membrane. Thiomers are capable of forming intra- and inter chain disulphide bonds within the polymeric network leading to strongly improved cohesive properties and stability of drug delivery systems such as matrix tablets. Due to the formation of strong covalent bonds with mucus glycoproteins, thiomers show the strongest mucoadhesive properties of all so far tested polymeric excipients via thioldisulphide exchange reaction and an oxidation process. They also exhibit permeation enhancing effects for the paracellular uptake of drugs based on a glutathione-mediated opening process of the tight junctions. So for those features matrix-tablets based on thiolated polymer present a promising type of buccal drug delivery systems.

Methods to study mucoadhesion[23]

The evaluation of mucoadhesive properties is fundamental to the development of novel Bioadhesive drug delivery system. Measurement of the mechanical properties of a Bioadhesive material after interaction with a substrate is one of the most direct ways to quantify the Bioadhesive performance. Testing is essential for the development, quantification, processing and proper use of the Bioadhesive. Several methods have been developed for the determination of Bioadhesive bond strength. These tests are also important during the design and development of Bioadhesive controlled release system as they ensure compatibility, physical and mechanical stability, surface analysis, and Bioadhesive strength. The test methods can be classified into two major categories:

***In vitro/Ex vivo* methods -*In vivo* methods *In vitro/Ex vivo* methods:** The *in vitro* methods are based on the measurements of either tensile stress or shear stress.

Methods based on measurement of tensile strength:

In these methods the force required to break the adhesive bond between a model membrane and the test polymer is measured.

Tensinometer:

This instrument consists of two jaws from flat glasses. The upper glass was fixed, but the lower glass had been mounted on a screw-elevating surface. The upper fixed glass was attached to a sensitive digital balance. Tablets from each formulation were suspended in water (pH 7) for 15 min. Then these adhesive tablets were located on the surface of lower glass and were elevated until they contact the surface of upper glass. The lower glass was then lowered until the tablet clearly was pulled free from the upper glass. The maximum tensile force needed to detach the jaws was recorded in gram/cm and mean values were calculated and recorded.

Modified balance method:

Modified double beam physical balance was used as the Bioadhesion test apparatus. The right pan of the balance was replaced with lighter one and pan was prepared with the Teflon ring hanging by a number of metallic rings. A cylinder at whose base a tablet was attached was hung from this ring. The two sides of the balance were then balanced with a fixed weight on the right hand side. The mucus membrane was tied with mucosal side upward using a thread over a Teflon block. The block was then lowered into the jacketed beaker which was then filled with phosphate buffer such that buffer just reached the surface of the balance. The balance beam was raised by removing the fixed weight kept on the right side of the pan. This lowered the Teflon cylinder along with the tablet over the mucosa. The balance was kept in this position for a fixed time and then slowly increased on the right pan till the tablet separated from the mucus surface. The excess weight on right hand side gave the Bioadhesive strength of the tablet in grams. It was observed that assembly gave reproducible results and performed efficiently.

In vitro methods

1. **Adhesion weight method:**

   A system where suspension of an exchange resin particles flowed over the inner mucosal surface of a section of guinea pig intestine and the weight of adherent particles was determined. Although the method has limited value due to poor data reproducibility resulting from fairly rapid degradation and biological variation of the tissue, it was possible to determine the effect of particle size and charge on the adhesion after 5 minutes contact with the adverted intestine.

2. **Flow channel method:**

   Mikos and Peppas developed this method which utilizes a thin channel made up of glass which is filled with 2% w/w aqueous solution of bovine submaxillary mucin, thermostated at 370C. Humid air at 370C was passed through glass channel. A particle of Bioadhesive

polymer was placed on the mucin gel, and its static and dynamic behaviour was monitored at frequent intervals using a camera, thereby calculating its adhesive property.

3. **Fluorescent probe method:**

In order to examine a large number of polymers for their Bioadhesive potential, the technique of labelling the lipid bilayer and memberane protein with the fluorescent probes namely pyrene and fluorescein isothiocynate, respectively, was used. Addition of polymers to this substrate

surface compressed the lipid bilayer or protein causing a change in fluorescence, as compared to control cells. By using the fluorescent probes, it was possible to compare charge type and density and backbone structure and their influence on polymer adhesion. Charged carboxylated polyanions were found to have a good potential for Bioadhesive drug delivery.

4. **Mechanical spectroscopic method:**

Mechanical spectroscopy was used to investigate the interaction between glycoprotein gel and polyacrylic acid, and the effect of pH and polymer chain length on this. Mortazavi et al., used a similar method to investigate the effect of carbopol 934 on the rheological behaviour of mucus gel. They also investigated the role of mucus glycoproteins and the effect of various factors such as ionic concentration, polymer molecular weight and its concentration, and the introduction of anionic, cationic and neutral polymers on the mucoadhesive mucus interface.

5. **Thumb test:**

It is simple test method used to quantify mucoadhesiveness. The difficulty of pulling the thumb from the adhesive as a function of pressure and contact time gives a measure of adhesiveness. It is most likely that any mucoadhesive system is adhesive to fingers, since most mucoadhesives are non-specific and not mucin specific and like mucin the skin has also many hydroxyl groups for interaction with Bioadhesive systems. Although the thumb test may not be conclusive, it provides useful information on mucoadhesive potential.

6. **Colloidal Gold Staining:**

This technique employed red colloidal gold particles, which were stabilized by the absorbed mucin molecules to form mucin gold conjugates. Upon interaction with mucin-gold conjugates, Bioadhesive hydrogel developed a red colour on the surface. Thus the interaction between them could easily be quantified, either by measurement of the

intensity of the red colour on the hydrogel surface or by the measurement of the decrease in the concentration of the conjugates from the absorbance changes at wavelength.

7. **Electronic conductance**:

   This method is used to test the semisolid mucoadhesive ointments. The adhesion of Orabase, carbopol, eudispert, guar gum and methylcellulose to artificial membranes in artificial saliva was studied by using a modified rotational viscometer capable of measuring electrical conductance. In the presence of adhesive the conductance was comparatively low, as the adhesive was removed, the value increased to final value, which corresponds to the conductance of saliva, which indicates the absence of adhesion.

Buccal Drug Delivery and Mucoadhesivity[24]:-

For the development of these Buccal drug delivery systems, mucoadhesion of the device is a key element. For proper and good mucoadhesion mucoadhesive polymer have been utilized in many different dosages form such as tablets, patches, tapes, films, semisolids and powders. Many studies showed that addition of various polymers to drug delivery systems such as gums, increased the duration of attachment of the formulations to the mucous surface and and also increased the efficacy. To serve as mucoadhesive polymers, the polymers should possess some general physiochemical features such as –

- Predominantly anionic hydrophilicity with numerous hydrogen bond-forming groups.
- Polymer and its degradation products should be non-toxic, non-irritant and free from leachable impuri-ties.
- Should have good spreadability, wetting, swelling and solubility and biodegradability properties.
- pH should be biocompatible and should possess good viscoelastic properties.
- Should possess peel, tensile and shear strengths at the bioadhesive range.

Classification of some mucoadhesive polymers are listed in **Table no- I.**

Types	**Example**
Natural and modified polymers	Agarose, Chitosan, Gelatin, Pectin, Sodium alginate, CMC, Na CMC, HPC, HPMC, Methyl cellulose.
Synthetic	Carbopol, Polycarbpphil, Polyacrilic acid,Polyacrylates.
Cationic and anionic	Aminodextran, Chitosan, Chitosan –EDTA, Dimethylaminoethyldextran

There are some Novel Mucoadhesive Polymers under development **,** these include Copolymer of PAA and PEG monoethylether monomethacrylate, PAA complexed with PEGylated drug conjugate, Hydrophilic pressure-sensitive adhesives (PSAs), AB block copolymer of

oligo(methyl methacrylate) and PAA , Polymers with thiol groups (cysteine was attached covalently to polycarbophil by using carbodiimide as a mediator.

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