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### A Review On Mucoadhesive Drug Delivery Systems

Payal Snehi<sup>1</sup>, Pranshu Tangri<sup>1</sup>, Pratima Jayasawal<sup>1</sup>, Jyoti Saxena<sup>1</sup>, Amrita Bisht<sup>1</sup>, N.G. Raghavendra Rao<sup>\*1</sup>

*Department of Pharmacy, GRD(PG)IMT, 214, Rajpur, Dehradun-248001, Uttarakhand, India.*

#### ABSTRACT

Since, the last four decades, the concept of mucoadhesion has achieved a much valuable interest in the various fields of pharmaceuticals. There are many advantages of mucoadhesive buccal drug delivery system that made this a novel drug delivery system for the local as well as systemic delivery of various drugs. The main advantage of this drug delivery system is that it prolongs the residence time of the dosage form at the site of application. Due to the high blood supply and relatively high permeability of the buccal mucosa, the buccal cavity is the best option for both local as well as systemic delivery of various drugs. The main prospect of writing this review article is to present comprehensive information related to mucoadhesion and mucoadhesive drug delivery systems. The article has highlighted all the aspects of mucoadhesive drug delivery systems which will be helpful for researches and academics. The article includes detailed information about mucosa- the anatomy and physiology, the mechanisms and theories related to mucoadhesion, evaluation parameters of mucoadhesive dosage forms, mucoadhesive polymers and novel approaches related to mucoadhesive drug delivery system. Drug actions can be improved by new drug delivery system, such as mucoadhesive system. This system remains in close contact with the absorption tissue, the mucous membrane, releasing the drug at the action site leading to improvement in both local and systemic effects. The potential merits and demerits of mucoadhesive drug delivery as well as that of the polymers are also discussed. It helps enhance the bioavailability through bypassing the first-pass metabolism effect. The mucosal surface better absorption and prolong resident time. Bioadhesion can be defined as the phenomenon of interfacial molecular attractive force in midst of the surface of the biological substrate and the natural or synthetic polymers, which allows the polymers to adhere to the biological surface for an extended period of time.

**Keywords:** Bio-adhesion, factors, mucosa, mucoadhesion, parameters, polymers.

\*Corresponding Author Email: [nraghu@rediffmail.com](mailto:nraghu@rediffmail.com), [drnraghu@gmail.com](mailto:drnraghu@gmail.com)

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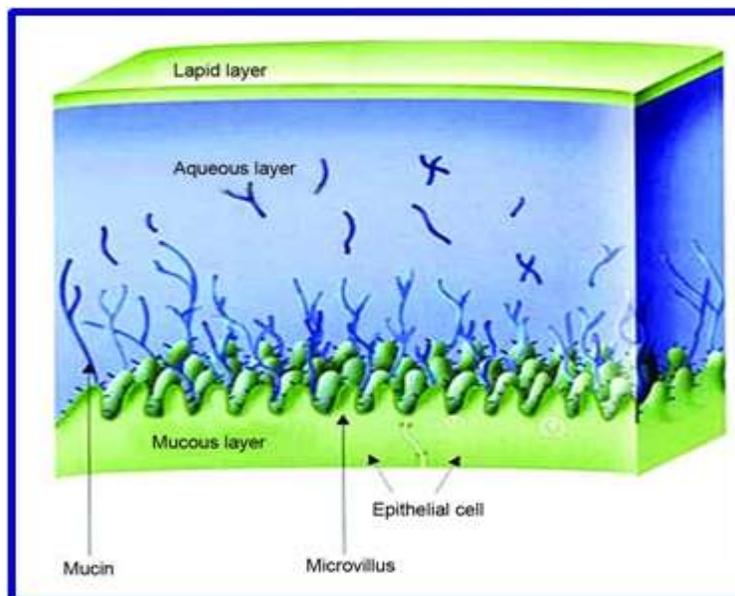
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## INTRODUCTION

Since from the last 40 years, the concept of mucoadhesion has provided the great application in prolonging the residence time as well as controlled release of various bioadhesive dosage forms through different mucosal routes. Formulations based on the mucoadhesive drug delivery system have shown the enhanced bioavailability of many drugs. use of various mucoadhesive polymers have achieved the significant interest in formulating the sustained release, extended release as well as prolonged release dosage forms. mucoadhesive drug delivery provides greater absorption and enhanced bioavailability of dosage forms due to the large surface area and higher blood in the mucosal cavities. Delivery across the mucus membrane provides various advantages over other drug delivery routes i.e., overcome the hepatic pass metabolism as well as the degradation of drugs by various gastrointestinal enzymes as well as intestinal oral<sup>[1]</sup>. For the desired mucoadhesive strength of the mucoadhesive dosage forms, there are various mucoadhesive polymers that can be used. Polymers are either natural or synthetic macromolecules which are capable of adhering to the mucosal surfaces. From last three decades, the use of various Mucoadhesive polymers has achieved a great interest in the of pharmaceutical technology. Nowadays, the use of mucoadhesive polymers has been accepted as an important strategy to prolong the residence time and to improve the localized of drug delivery systems on various mucus membranes<sup>[2]</sup>.

### **Mucus Membranes:**

Mucus membranes (mucosae) [Fig 1] are the moist surfaces lining the walls of various body cavities such as the gastrointestinal and respiratory tracts. They consist of a connective tissue layer (the lamina propria) above which is an epithelial layer, the surface of which is made moist usually by the presence of a mucus layer. The epithelia may be either single layered (e.g. the stomach, small and large intestines and bronchi) or multilayered/stratified (e.g. in the esophagus, vagina and cornea). The former contain goblet cells which secrete mucus directly onto the epithelial surfaces; the latter contain, or are adjacent to tissues containing, specialized glands such as salivary glands that secrete mucus onto the epithelial surface. Mucus is present either as a gel layer adherent to the mucosal surface or as a luminal soluble or suspended form. The major components of all mucus gels are mucin glycoproteins, lipids, inorganic salts and water, the latter accounting for more than 95% of their weight, making them a highly hydrated system<sup>[3]</sup>. The major functions of mucus are that of protection and lubrication.



**Figure 1: Mucus membrane structure**

An immediate release dosage form is administered using a fixed dosing interval which causes several potential problems as like saw tooth kinetics characterized by large peaks and troughs in the drug concentration-time curve frequent dosing for drugs with short biologic half-life, and above all the patient noncompliance. Controlled release (CR) DDS attempt to sustain drug blood concentration at relatively constant and effective levels in the body by spatial placement or temporal delivery. The idea of mucoadhesion stems from the need to localize drugs at a specific region of body (e.g stomach) because many drugs show poor bioavailability (BA) in the presence of intestinal metabolic enzymes like cytochrome P450 (CYP3A), abundantly present in the intestinal epithelium. potential candidates for drug delivery by mucoadhesive dosage form to different sites includes oral, gastrointestinal, nasal, ocular, vaginal, and rectal. A brief comparison was discussed about these sites for drug delivery. Buccal route found to be more suitable for the delivery of pharmaceutical agents using mucoadhesive polymers due to presence of relatively static and smooth surface on which various mucoadhesive dosage forms can be placed. Different dosage forms like lms, tablets, gels, ointments and patches can be used for delivery of drug across the buccal mucosa. Drugs may be suitable candidates to be delivered via the oral cavity which are having short biological half-life, poor solubility and permeability, susceptible to enzymatic degradation and for achieving sustain release etc. Another important site is nasal route for mucoadhesive formulations. It has a large surface area of about 150-200 cm. activity of mucociliary layer enhanced by presence of any foreign particle matter, therefore the residence time of particles in nasal mucosa varies between 15-30 min by employing various mucoadhesive formulations the residence time of the drug can be enhanced. Topical delivery of drugs to the eye is most important route for the treatment of various eye related

disorders. For achieving the effective delivery of therapeutic agents to the eye, various dosage forms such as eye-drops, ointments, gels and ocular inserts can be utilized. Due to effective protective mechanism of the eye, the bioavailability of many drugs is very poor. lachrymation, drainage and blinking of eyes remove drugs from the eye's surface rapidly. is problem can be overcome by employing mucoadhesive polymers like poloxamer, methyl cellulose, PVP, CAP, PAMAM and thiolated PAA. Mucoadhesive dosage form have also employed for delivery of drugs through rectal and vaginal routes. routes have several advantages like pain avoidance, tissue damage avoidance, first pass metabolism avoidance, and decrease in hepatic side effects which are found very common during parenteral route of administration. polymers used for delivery of drugs through rectal and vaginal routes are gelatin, mucin, poloxamer and polycarbophil. Various rectal and vaginal formulations include creams, ointments, in-situ gels, emulgels, tablets<sup>[4]</sup>.

### **Mechanisms of Mucoadhesion:**

The mechanism of mucoadhesion is generally divided into two steps: the contact stage and the consolidation stage [Fig 2]. The first stage is characterized by the contact between the mucoadhesive and the mucus membrane, with spreading and swelling of the formulation, initiating its deep contact with the mucus layer<sup>[5]</sup>. In the consolidation step [Fig 2], the mucoadhesive materials are activated by the presence of moisture. Moisture plasticizes the system, allowing the mucoadhesive molecules to break free and to link up by weak Vander Waals and hydrogen bonds. Essentially, there are two theories explaining the consolidation step: the diffusion theory and the dehydration theory. According to the diffusion theory, the mucoadhesive molecules and the glycoproteins of the mucus mutually interact by means of interpenetration of their chains and the building of secondary bonds. For this to take place, the mucoadhesive device has features favoring both chemical and mechanical interactions. For example, molecules with hydrogen bond building groups (-OH, -COOH), an anionic surface charge, high molecular weight, flexible chains and surface-active properties, which help in spreading throughout the mucus layer, can present mucoadhesive properties.

Usually four categories of bio-adhesion have been notable within the biological process. They are commonly stated as a unification of (i) a normal cell to a further normal cell; (ii) a standard common cell to a pathological cell (iii) a cell to a foreign matter; and (iv) an bonding agent to biological substances. In case of mucoadhesion, the foremost phase includes a friendly get in touch with a muco-adhesive material as well as mucus or a biological membrane by each, because of a superior wetting or swelling of the bio-adhesive. The overall mechanism basically includes creation of mucoadhesive bond. Broadly the stages of mucoadhesion composed of two important stages[Fig 3] i.e. contact stage (primary) and consolidation stage (secondary).

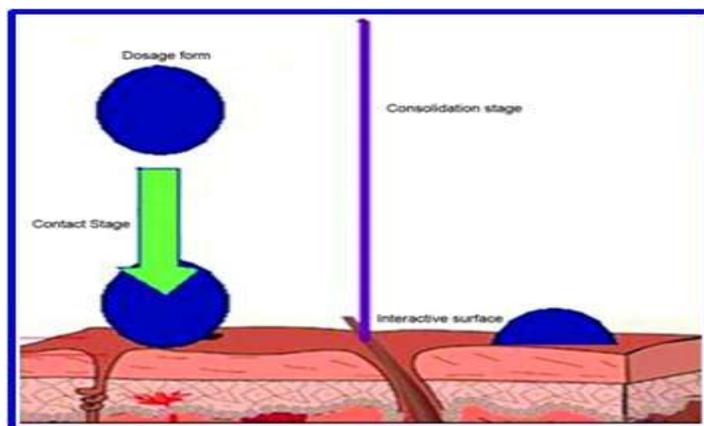
**Step I (contact stage):** It involves the wetting and consequently swelling of the bioadhesive or polymer which takes place when a polymer is placed on the mucous membrane and results in to a deep contact. Here polymer swelling arises since the substances of polymer have an attraction for water<sup>[6]</sup>.

**Step II (polymer chains and mucosal membrane Interpenetration):** Just like that in the second phase, the polymer chains of mucoadhesive and the mucosal layer can interact and entangles by formation of adhesive bonds. Later on the contact has been recognized and perforation of the bioadhesive into the crevices of tissue exterior portion. Afterwards a correlation exists and bioadhesive chains impregnate with those of mucus. This phenomenon also had been occurred by force of bonds which rely on extent of perforation among two polymer groups<sup>[7]</sup>.

**Step III (bonds creation among the entwined chains):** Here both collectively recognized as consolidation stage. In this case, the weak chemical bonds can resolve at that time which was depicted in [Fig 4]. Other types of bond comprise covalent bonds and secondary interactions like hydrogen bonds as well as Vander Waals bonds. Figure 1. Steps involved in mechanism of mucoadhesion<sup>[8]</sup>.

#### Factors affecting mucoadhesion [Fig 5]:

- Polymer related factors: Several properties or characteristics of the active polymer play a vital role in mucoadhesion. Among them, polymer molecular weight, concentration, swelling, of polymer chains flexibility, and particular confirmation which may affect the mucoadhesion.
- Environment associated factors: pH of the polymer substrate interface, functional strength and first contact time is able to influence the mucoadhesion.
- Physiological factors: Disease state and mucine turn over are the important physiological factors, which can also affect mucoadhesion.



**Figure 2: The process of contact and consolidation**

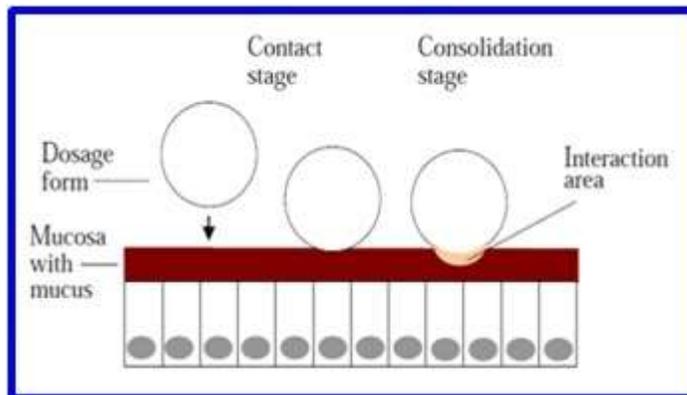


Figure 3: The two stages in mucoadhesion

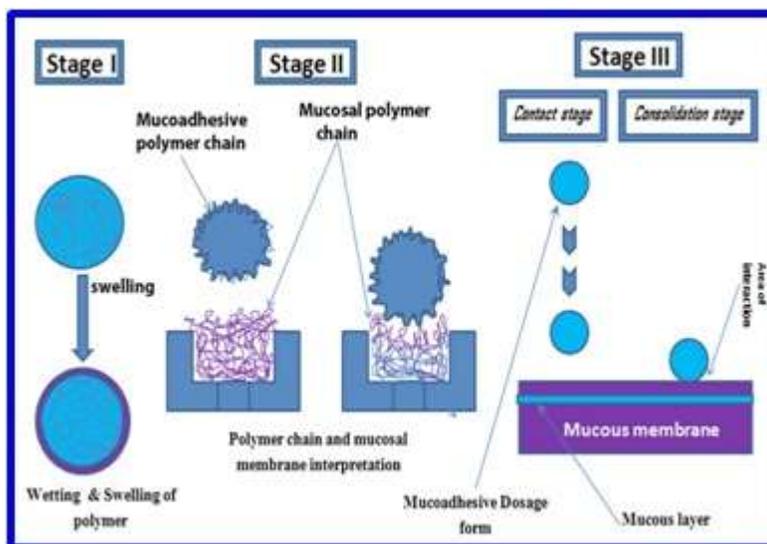


Figure 4: Steps involved in mechanism of mucoadhesion.

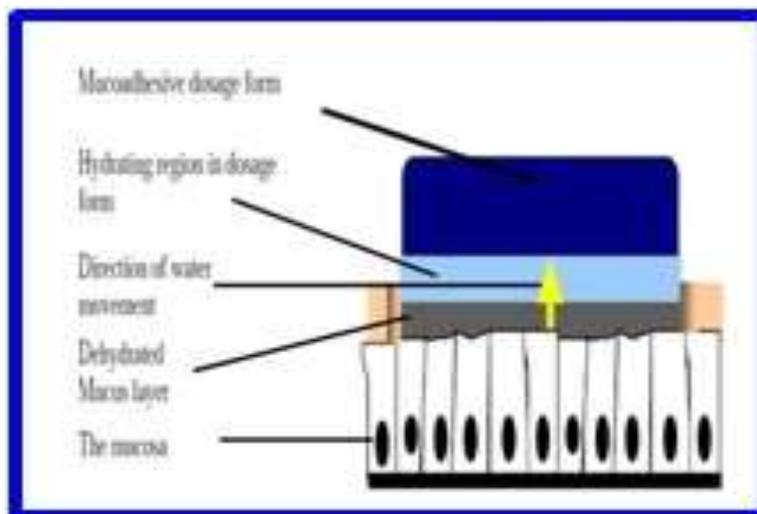


Figure 5: The dehydration theory of mucoadhesion

Advantages of Mucoadhesive Drug Delivery Systems<sup>[9]</sup>

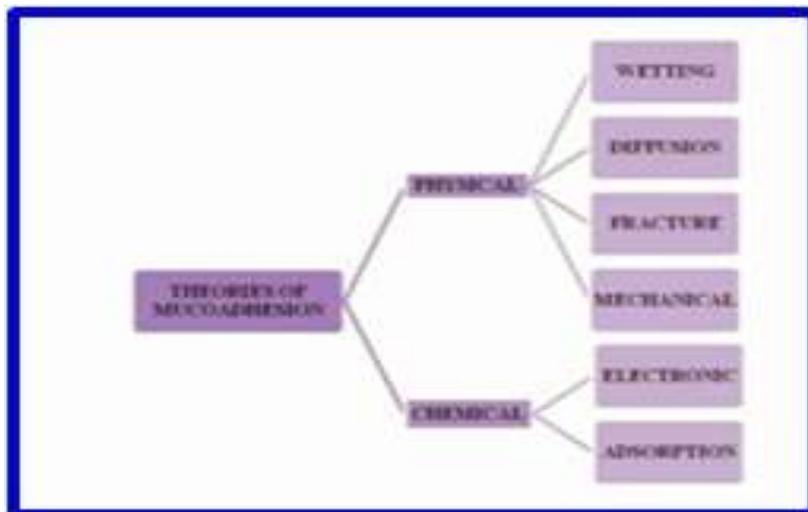
- Increases the residence time of formulation at the site of absorption, hence surges the bioavailability.
- Excellent accessibility, rapid onset of action possible.
- Quick absorption because of tremendous blood supply and good perfusion rates.
- Better patient compliance.
- Rapid healing and cellular recovery of the local site.
- Lower dosing frequency.
- Short treatment period.
- Increased margin of safety for highly potent drugs due to improved control of plasma level concentration.
- Maximum utilization of drug enabling reduction in total quantity of drug administered.

**Disadvantages of Mucoadhesive Drug Delivery Systems:** <sup>[10-16]</sup>

- The dissolution of drug due to continuous secretion of saliva (0.5-2 l/day)
- Prolonged contact of the drug possessing ulcerogenic property.
- For the in vitro screening of drugs the oral mucosal delivery is lack of good model. This is the major drawback of this drug delivery.
- Patient acceptability in terms to taste, irritancy and mouth feel is to be checked.
- Also has smaller surface area.
- Costly drug delivery system.
- One of the major limitations in the development of oral mucosal delivery is the lack of a good model for in vitro screening to identify drugs suitable for such administration.
- Eating and Drinking is prohibited.

**Theories of Mucoadhesion:**

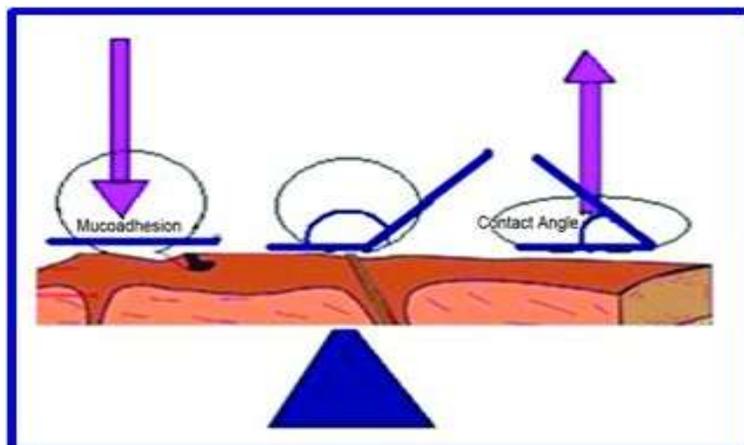
**Bonding Mechanism** There are six traditional theories which have resulted from studies on the performance of variety of materials and polymer- polymer adherence. The classification of these theories is shown. The contact angle and time of contact plays a significant role in mucoadhesion as shown in [Fig 6].



**Figure 6: Role in mucoadhesion**

### Wetting theory:

The affinity between the liquid systems and the mucus membrane is obtained by ascertaining the contact angle [Fig 7]. As a basic concept, as the contact angle decreases, the affinity increases. The contact angle must be near to zero to provide sufficient Spreadability. The Spreadability coefficient,  $SAB$ , is measured from the difference between the surface energies  $\gamma_B$  and  $\gamma_A$  and the interfacial energy  $\gamma_{AB}$ , as indicated in equation:  $SAB = \gamma_B - \gamma_A - \gamma_{AB}$ . Higher the individual surface energy of mucus and device in relation to the interfacial energy, more is the work of adhesion, <sup>[17]</sup>



**Figure 7: Influence of contact angle on mucoadhesion**

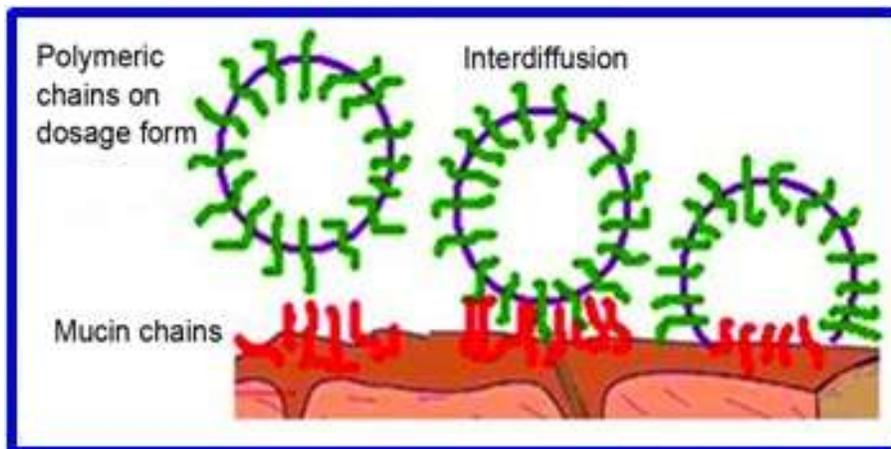
### Diffusion theory:

The diffusion theory explains the phenomenon of the interpenetration and entanglement of the bioadhesive polymer chains and mucous polymer chains. As the bond strength enhances, the degree of the penetration increases. The secondary interactions [Fig 8] due to inter-diffusion can be seen in Diffusion coefficient, polymer chain flexibility, nature of mucoadhesive chains, mobility and contact time of polymer chains are the factors on which the degree of penetration depends. The depth of

interpenetration required to produce a firm bio adhesive bond lies in the range 0.2–0.5  $\mu\text{m}$ . This depth of interpenetration of polymer and mucin chains can be found out by the following equation:  
The interpenetration depth,

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

Where  $t$  = contact time and  $D_b$  = diffusion coefficient of the mucoadhesive material in the mucus.

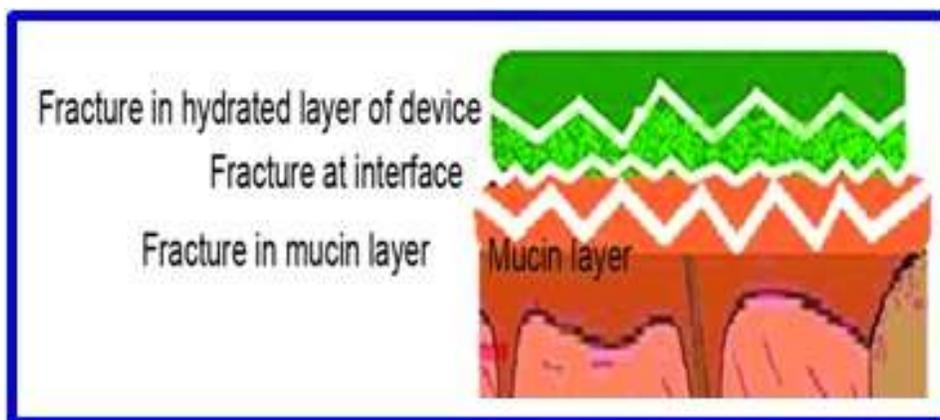


**Figure 8: Secondary interaction between mucoadhesive device and of mucus**

#### Fracture theory:

This theory examines the force needed to dissociate two surfaces after adhesion is established [Fig 9]. The work of fracture has been found to rise when the polymer network fibres are longer or if the degree of cross-linking within such a system is decreased. This concept aids in the measurement of fracture strength ( $\sigma$ ) after the separation of two surfaces via its relationship to the Young's modulus of elasticity ( $E$ ), the fracture energy ( $\epsilon$ ) and the critical crack length ( $L$ ) through the following equation:  $\sigma = (E \cdot \epsilon / L)^{1/2}$ . The force,  $S_m$ , is frequently calculated in tests of resistance to rupture by the ratio of the maximal detachment force,  $F_m$ , and the total surface area,  $A_0$ , involved in the adhesive interaction:

$$S_m = F_m / A_0$$



**Figure 9: Fractures occurring for mucoadhesion**

**Mechanical theory:**

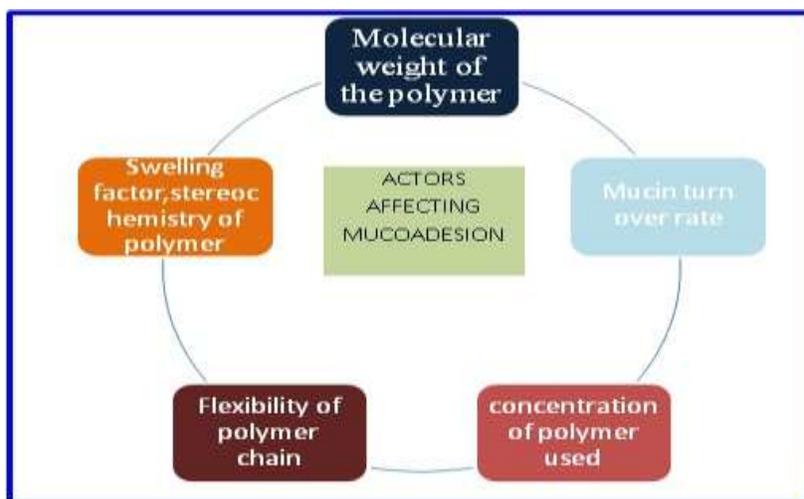
Mechanical theory proposes that the adhesion is because of the filling of the imperfections of a rough surface by a mucoadhesive liquid. The irregularity enhances the interfacial area available for interactions thus enhancing energy dissipation. The mechanisms ruling mucoadhesion are also determined by the intrinsic properties of the formulation and by the environment in which it is applied. Intrinsic factors of the polymer are related to its molecular weight, concentration and chain flexibility. For linear polymers, mucoadhesion is directly proportional to molecular weight, but the same does not hold for non-linear polymers.

**Electronic theory:**

The electronic theory relies on the hypothesis that the bioadhesive material and the target mucous membrane have diverse attributes of electronic surface. Based on this, when the surfaces come in contact with each other, there is an electron transfer to balance the Fermi levels, arising due to the formation of electrical double layer at the interface of the bioadhesive and the mucous membrane. The bioadhesive force is assumed to be present due to the attractive forces over this double layer.

**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. Various mucoadhesive interactions are: Ionic bonding, Covalent bonding, Hydrogen bonding, Van der Waals bonding, Hydrophobic bonding. For example, hydrogen bonds are the dominant interfacial forces in polymers having carboxyl groups. These forces are very important in the adhesive interaction phenomena because they might be individually weak, a great number of interactions can result in a strong global adhesion<sup>[18]</sup>.

**FACTOR AFFECTING MUCOAHESION:****Classification of buccal bio-adhesive dosage form:**

**Buccal Bio-adhesive Tablets:**

Buccal bioadhesive tablets are dry dosage forms that are to be moistened after placing in contact with buccal mucosa. Double and multilayered tablets are already formulated using bioadhesive polymers and excipients. These tablets are solid dosage forms that are prepared by the direct compression of powder and can be placed into contact with the oral mucosa and allowed to dissolve or adhere depending on the type of excipients incorporated into the dosage form. They can deliver drug multi- directionally into the oral cavity or to the mucosal surface.

**Buccal Bio-adhesive Semisolid Dosage Forms:**

Buccal bioadhesive semisolid dosage forms consist of finely powdered natural or synthetic polymers dispersed in a polyethylene or in aqueous solution example: Arabase. Buccal Bioadhesive Patches and Films Buccal bioadhesive patches consists of two ply laminates or multilayered thin film that are round or oval in shape, consisting of basically of bioadhesive polymeric layer and impermeable backing layer to provide unidirectional flow of drug across buccal mucosa. Buccal bioadhesive films are formulated by incorporating the drug in alcohol solution of bioadhesive polymer.

**Buccal Bio-adhesive Powder Dosage Forms:**

Buccal bioadhesive powder dosage forms are a mixture of bioadhesive polymers and the drug and are sprayed onto the buccal mucosa the reduction in diastolic B.P after the administration of buccal tablet and buccal film of Nifedipine. Buccal chewing gum Some commercial products of buccal chewing gum are available in the market 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<sup>[19]</sup>.

**Bio-adhesive 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 buccal spray was approved for commercial marketing and sales in Ecuador.

**Physiological factors affecting buccal bioavailability:**

**Inherent permeability of the epithelium:** The permeability of the oral mucosal epithelium is intermediate between that of the skin epithelium, which is highly specialized for barrier function and the gut, which is highly specialized for an adsorptive function. Within the oral cavity, the buccal mucosa is less permeable than the sublingual mucosa.

**Thickness of epithelium:** The thickness of the oral epithelium varies considerably between sites in the oral cavity. The buccal mucosa measures approximately 500- 800µm in thickness.

**Blood supply:** A rich blood supply and lymphatic network in the lamina propria serve the oral cavity, thus drug moieties which traverse the oral epithelium are readily absorbed into the systemic circulation. The blood flow in the buccal mucosa is 2.4ml. Metabolic activity Drug moieties adsorbed via the oral epithelium are delivered directly into the blood, avoiding first pass metabolism effect of the liver and gut wall. Thus oral mucosal delivery may be particularly attractive for the delivery of enzymatically labile drugs such as therapeutic peptides and proteins.

**Saliva and mucous:** The activity of the salivary gland means that the oral mucosal surfaces are constantly washed by a stream of saliva, approximately 0.5-2L per day. The sublingual area in particular, is exposed to a lot of saliva which can enhance drug dissolution and therefore increase bioavailability.

**Ability to retain delivery system:** The buccal mucosa comprises an expanse of smooth and relatively immobile surface and thus is ideally suited to the use of retentive delivery systems. Species differences Rodents contain a highly keratinized epithelium and thus are not very suitable as animal models when studying buccal drug delivery [20].

**BIOADHESIVE POLYMERS:**

The second step in the development of buccoadhesive dosage forms is the selection and characterization of appropriate bioadhesive polymers in the formulation." Bioadhesive polymers play a major role in buccoadhesive drug delivery systems of drugs. Polymers are also used in matrix devices in which the drug is embedded in the polymer matrix, which controls the duration of release of drugs an ideal polymer for buccoadhesive drug delivery systems should have following Characteristics.

**TYPES OF POLYMERS:**

Mucoadhesive drug delivery systems are based on the adhesion of a drug/ carrier to the mucous membrane. To promote this adherence a suitable carrier is required.

**Ideal Characteristics of Mucoadhesive Polymers:**

A mucoadhesion promoting agent or the polymer is added to the formulation which helps to promote the adhering of the active pharmaceutical ingredient to the oral mucosa. The agent can have such additional properties like swelling so as to promote the disintegration when in contact with the saliva.

1. Polymer must have a high molecular weight up to 100.00 or more. This is necessary to promote the adhesiveness between the polymer and mucus.
2. Long chain polymers-chain length must be long enough to promote the interpenetration and it should not be too long that diffusion becomes a problem.
3. High viscosity.
4. Degree of cross linking- it influences chain mobility and resistance to dissolution. Highly cross linked polymers swell in presence of water and retain their structure. Swelling favours controlled release of the drug and increases the polymer/mucus interpenetration
5. Spatial conformation.
6. Flexibility of polymer chain- this promotes the interpenetration of the polymer within the mucus network.
7. Concentration of the polymer- an optimum concentration is required to promote the mucoadhesive strength. It depends however, on the dosage form.
8. Charge and degree of ionization- the effect of polymer charge on mucoadhesion was clearly shown by Bernkop-Schnurch and Freudl. Cationic chitosan HCl showed marked adhesiveness when compared to the control. The attachment of EDTA an anionic group increased the mucoadhesive strength significantly. DTPA/chitosan system exhibited lower mucoadhesive strength than cationic chitosan and anionic EDTA chitosan complexes because of low charge. Hence the mucoadhesive strength can be attributed as anion>cation>non-ionic.
9. Optimum hydration- excessive hydration leads to decreased mucoadhesive strength due to formation of a slippery mucilage.
10. Optimum pH – mucoadhesion is optimum at low pH conditions but at higher pH values a change in the conformation occurs into a rod like structure making those more available for inter diffusion and interpenetration. At very elevated pH values, positively charged polymers like chitosan form polyelectrolyte complexes with mucus and exhibit strong mucoadhesive forces.
11. It should non toxic, economic, biocompatible preferably biodegradable<sup>[21]</sup>.
12. It should be inert and compatible with the environment

13. The polymer and its degradation products should be non-toxic absorbable from the mucous layer.
14. It should adhere quickly to moist tissue surface and should possess some site specificity.
15. The polymer must not decompose on storage or during the shelf life of the dosage form.
16. The polymer should be easily available in the market and economical.

**Various mucoadhesive polymers can broadly be categorized as follow:**

**Synthetic polymers:**

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

**Natural polymers:**

Tragacanth, Sodium alginate, Guar gum, Xanthum gum, soluble starch, Gelatin, Chitosan.

**Mucoadhesive polymers can also classify into following categories:**

**Traditional non-specific first-generation mucoadhesive polymers**

First-generation mucoadhesive polymers may be divided into three main subsets, namely:

- 1) Anionic polymers,
- 2) Cationic polymers,
- 3) Non-ionic polymers.

Of these, anionic and cationic polymers have been shown to exhibit the greatest mucoadhesive strength. Consequently, such charged polymeric systems will now be examined in more depth.

**1. Anionic polymers:**

Anionic polymers are the most widely employed mucoadhesive polymers within pharmaceutical formulation due to their high mucoadhesive functionality and low toxicity. Typical examples include poly (acrylic acid) (PAA) and its weakly cross-linked derivatives and sodium carboxymethylcellulose (NaCMC). PAA and NaCMC possess excellent mucoadhesive characteristics due to the formation of strong hydrogen bonding interactions with mucin. Polycarbophil (Noveon) and Carbomers (Carbopol), PAA derivatives have been studied extensively as mucoadhesive platforms for drug delivery to the GI tract.

**2. Cationic Polymers:**

Of the cationic polymer systems, undoubtedly chitosan is the most extensively investigated within the current scientific literature. Chitosan is a cationic polysaccharide, produced by the deacetylation of chitin, the most abundant polysaccharide in the world, next to cellulose. The intriguing properties of chitosan have been known for many years with many examples of its use in agriculture, industry and medicine<sup>[22]</sup>.

#### **Novel second-generation mucoadhesive:**

The major disadvantage in using traditional non-specific mucoadhesive systems (first generation) is that adhesion may occur at sites other than those intended. Unlike first-generation non-specific platforms, certain second-generation polymer platforms are less susceptible to mucus turnover rates, with some species binding directly to mucosal surfaces; more accurately.

**Lectin:** The most widely investigated of such systems in this respect are lectins. Lectins belong to a group of structurally diverse proteins and glycoproteins that can bind reversibly to specific carbohydrate residues. After initial mucosal cell-binding, lectins can either remain on the cell surface or in the case of receptor-mediated adhesion possibly become internalised via a process of endocytosis.

#### **Thiolated polymers:**

The presence of free thiol groups in the polymeric skeleton helps in the formation of disulphide bonds with that of the cysteine-rich sub-domains present in mucin which can substantially improve the mucoadhesive properties of the polymers (e.g. poly (acrylic acid) and chitosan). Various thiolated polymers include chitosan-iminothiolane, poly(acrylic acid), cysteine, poly (acrylic acid), homocysteine, chitosan-thioglycolic acid, chitosan thioethylamidine, alginate-cysteine, poly (methacrylic acid), cysteine and sodium carboxymethylcellulose-cysteine.

#### **Polyox WSR:**

A class of high molecular weight polyethylene molecular weight polyethylene oxide homopolymers having the following properties,

- Water soluble hydrophilic nature
- Functional group for hydrogen bonding
- Biocompatible and non toxic
- High molecular weight

#### **Novel polymers:**

Tomato lectin showed that it has binding selectivity to the small intestine epithelium.

A new class of hydrophilic pressure sensitive adhesives (PSA) have been developed by corium technologies. Complex have been prepared by non covalent hydrogen bonding crosslinking of a film

forming hydrophilic polymer with a short chain plasticizer having reactive OH groups at chain ends<sup>[21]</sup>.

**Backing membrane:** Backing membrane plays a major role in the attachment of bioadhesive devices to the mucus membrane. The materials used as backing membrane should be inert, and impermeable to the drug and penetration enhancer. The commonly used materials in backing membrane include carbopol, magnesium separate, HPMC, HPC, CMC, polycarbophil etc. The main function of backing membrane is to provide unidirectional drug flow to buccal mucosa. It prevents the drug to be dissolved in saliva and hence swallowed avoiding the contact between drug and saliva. The material used for the backing membrane must be inert and impermeable to drugs and penetration enhancers.

**Penetration enhancers:** To increase the permeation rate of the membrane of co-administered drug they are added in the pharmaceutical formulation. Without causing toxicity and damaging the membrane they improve the bioavailability of drugs that have poor membrane penetration. The capability to enhance the penetration is dependent upon they are used in combination or alone, nature of vehicle<sup>[23-25]</sup>.

## CONCLUSION:

This overview about the mucoadhesive dosage forms might be a useful tool for the efficient design of novel mucoadhesive drug delivery systems. Mucoadhesive drug delivery systems have applications from different angles, including development of novel mucoadhesives, design of the device, mechanisms of mucoadhesion and permeation enhancement. Scientists are trying to improve the bioavailability of active agents by tailoring the properties of the delivery systems instead of designing new active agents. Mucoadhesive polymers may provide an important tool to improve the bioavailability of the active agent by improving the residence time at the delivery site. The various sites where mucoadhesive polymers have played an important role include buccal cavity, nasal cavity, rectal lumen, vaginal lumen and gastrointestinal tract. Development of novel mucoadhesive delivery systems are being undertaken so as to understand the various mechanism of mucoadhesion and improved permeation of active agents. The mucoadhesive drug delivery system is a cumulative for delivering the drugs which have narrow absorption window at the target site to optimize their usefulness. Many potential mucoadhesive systems are being investigated which may find their way into the market in the near future.

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