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Abstract: The mucus layer that covers the mucosal epithelial surface and mucin molecules interact with mucoadhesive drug delivery methods to prolong the duration the dosage form spends at the absorption site. This review addresses the mechanisms and theories underlying mucoadhesion, the influences on mucoadhesive devices, as well as numerous mucoadhesive dose forms. By creating innovative drug delivery methods, drug effects can be improved. Several in vitro and in vivo methodologies are suggested for understanding its mechanisms. Through a variety of contact methods, the mucoadhesive formulation can stick to the mucosal membrane and improve the retention and permeability of bioactive substances. Bioactive substances can be absorbed from the mucosa, which avoids the hepatic first-pass metabolism and gastrointestinal transit, to increase bioavailability. The food industry accepts a variety of mucoadhesive polymers, emulsifiers, and thickeners used in pharmaceutical formulation. In the nutraceutical industry, the introduction of mucoadhesive formulations will be a game-changer because we are still exploring new strategies to increase the bioavailability of several bioactive substances.

Mucoadhesive drug delivery systems may be affected by the mucus barrier, which covers mucin molecules and the mucosal epithelial surface. This interaction lengthens the dose form's stay at the site of absorption, boosting therapeutic outcomes and drug bioavailability and effectiveness. In order to improve the pattern of drug release, solubility, and dissolution of medications that are insufficiently soluble, polymers are utilized to give muco-adhesion to the dosage form. Using interfacial forces, two components, one of which is biological, can be held together for long periods of time in a condition known as Mucoadhesions.

The mucosa has a lot of blood flow and is fairly permeable. Readers will gain a better grasp of this medication delivery technique, its formulation options, and its benefits and drawbacks after reading this review. Bypassing the first-pass effect, a novel drug delivery technique known as buccal drug delivery allows the medication to reach the systemic circulation quickly.

Key word: MDDS , Mucoadhesion, Bioadhesion, Control Drug Release

Introduction: Drug delivery methods that are mucoadhesive interact with mucin molecules and the mucus layer that covers the mucosal epithelial surface to prolong the period that the dose form remains at the site of absorption. The controlled medication delivery system includes a mucoadhesive drug delivery system. Developing a unique medication delivery method. medication administration through the absorptive mucosa of several easily accessible bodily cavities, including the ocular, Compared to peroral administration, nasal, buccal, rectal, and vaginal mucosa presented definite advantages for overall effect. The dosage form's time spent at the site of administration is extended by mucoadhesive drug delivery systems. applying or absorbing. They make it possible for the dose form to have close contact with the underlying absorption surface, enhancing the drug's therapeutic efficacy.

For mucoadhesive medication delivery, dosage forms must be tiny and flexible enough to be accepted by patients and not irritate them. A mucoadhesive dosage form is also desirable for its high drug loading capacity, regulated medication release (ideally in one direction). high mucoadhesive capacity, tastelessness, a smooth surface, and easy application. For a range of medications, several pertinent mucoadhesive dose forms have been created, a number of peptides. Including insulin, octreotide, and thyrotropin-releasing hormone (TRH), Leuprolide and oxytocin have been administered through the mucosal route, however with only moderate success. Due to their hydrophilicity and high molecular weight, as well as the low (0.1–5%) bioavailability intrinsic mucosal permeability and enzymatic barriers.

The goal of developing a sustained release dosage form is to release the medication gradually over an extended period of time, yet this is insufficient to obtain a prolonged therapeutic impact. They can leave the absorption site before the medication substance is released.

The mucoadhesive dosage form will instead serve the dual functions of sustained release and dosage form presence at the site of absorption. Our review highlights a few mucoadhesive drug delivery technologies in this regard. The mucoadhesive dosage form will instead serve the dual functions of sustained release and dosage form presence at the site of absorption. Our review highlights a few mucoadhesive drug delivery technologies in this regard.

History:
The idea of mucoadhesion has attracted a lot of attention since the early 1980s. pharmaceutical engineering. Adhesion is the binding created by contact between two objects.
A surface, along with pressure-sensitive adhesive. In accordance with the American Society of Testing and Material the situation where two surfaces are kept together by interfacial forces, which may consist of interlocking forces, valence forces, or both. Due to its remarkable approachability, ability to avoid first-pass metabolism, big blood supply, safety, and increased patient satisfaction during the past several years, the mucoadhesive drug delivery method has grown in popularity and received significant attention for both local and systemic medicine delivery.

Acceptance with improved and better care. T.R. Jacoby and colleagues attempted to create a bio-adhesive penicillin ointment in 1947. using gum tragacanth for topical purposes gave rise to the concept of developing medicinal products made with mucoadhesive polymers. The mucus layer and a bioadhesive polymer interact during the process of muco-adhesion. covering the areas of the body that were wet. interpenetration and absorption of the concerned. There are chains of biopolymers. The situation in which two materials, at least one of which is biological in nature, are held together by interfacial forces over lengthy periods of time is known as bioadhesion. When one of the components is a mucus membrane (biological), mucoadhesion occurs then another is a natural or artificial polymer that is kept together for a long time by interfacial force.

**Anatomy and physiology of the mucosa:**
The oral mucosa is sticky by nature and functions as a lubricant, allowing the cells to move in comparison to one another less gratefully. The oral mucosa primarily has three functioning zones:
1) The gingiva and hard palate are covered by the masticatory mucosa, which accounts for 25% of the total oral mucosa. epithelium with keratinization.
2) Lining mucosa: This mucosa encompasses the lips, cheeks, soft palate, and 60% of the entire oral mucosa. The floor of the oral cavity and the lower surface of the tongue. mucosa that is not keratinized.

**Regional Differences In Mucosal Permeability**
Permeability: Intermediate between epidermis & intestinal mucosa
Permeability of oral mucosa: sublingual > buccal > palate

**Mucoadhesive drug delivery system**
Drug delivery methods that interface with the mucosal layer to prolong their residence duration at the administration site for improved absorption are known as mucoadhesive drug delivery systems. These systems are developed to deliver a drug's controlled or sustained release at the location of administration.

**Principle of mucoadhesion drug delivery system:**
The principle of mucoadhesion drug delivery system is based on mucoadhesion and bioadhesion. The drug delivery system is fixed on the chemical with a standard adhesion layer called "bioadhesion". Bioadhesion is the ability of materials (synthetic or biological) to adhere to tissue for a long time. When these adhesion interactions are limited to the mucus layer on the mucosal surface, it is called "mucoadhesion". The interfacial molecular attraction between the two parts of the biomatrix and natural or synthetic polymers allows the polymers to act as biological materials for long periods of time.

Give special effects to the place by placing the medicine in special places. The relationship with the mucosa increases the duration depending on the prescription in a single area.

**Bioadhesion Principle:**
In traditional chemistry, it is believed that in order for molecules to stick, they must combine with the following bonds at the interfaces:
1) Ionic Bonds: These are formed by the combination of two opposite substances, ions. Strong bonds attract each other through electrostatic interactions (e.g. in solids).
2) Covalent Bonds: These strong bonds are formed when pairs of electrons are shared between atoms to fill the orbitals of both.
3) Hydrogen Bonds: These bonds are generally weaker than ionic or covalent bonds. Hydrogen atoms have a slightly positive charge, so they are attracted to and bond with electronegative atoms such as oxygen or nitrogen.
4) Van der Waals bonds: These are some of the negative interactions. They arise from dipole-dipole and dipole-induced dipole attractions in polar molecules and dispersion forces in non-polar substances.

5) Hydrophobic Bonds (Hydrophobic Effect): These are also the weakest interactions. Indirect bonds occur when nonpolar groups are present in aqueous solution (these groups only resemble each other). Water molecules adjacent to non-polar groups reduce the entropy of the system by forming hydrogen bond structures. Therefore, in order to reduce this effect, the tendency of non-polar groups to establish relationships with each other increases.

Mucosal Drug Delivery Systems desired Features: Rapid adhesion to the mucosa without changing the physical properties of the body.
1. It should not interfere with the administration/release of the active substance.
2. It should be biodegradable and not produce any toxic by-products.
3. Workers' permeability should be improved.
4. The formulation lasts longer at the delivery site and increases the bioavailability of the API.
5. Specific bioadhesion drugs can target specific areas or tissues.
6. The use of antibiotics can alter tissue permeability to allow the passage of larger particles such as peptides and proteins.
   - First. Sodium glycocholate, sodium taurocholate and L-lysocephatidylcholine
7. The use of protease inhibitors in mucoadhesive drugs allows better absorption of peptides and proteins.

Classification of mucoadhesive drug delivery systems:
A. Non-adhesive mucosal delivery systems:
   (a) These systems are designed for absorption through the mucosa in the oral cavity. For example: sublingual tablets, fast-dissolving tablets (orally dissolving tablets or orally insoluble tablets), etc.
B. Connect or repair mucosal drug delivery systems:
   (b) This system is designed to pass through them. Adhesive properties It binds to the mucosal surface.
   (c) These systems are also known as mucoadhesive systems. For example: oral delivery system, rectal delivery system, vaginal delivery system, nasal delivery system etc.

Types of Mucoadhesive drug delivery system:
While in bioadhesion the polymer is coupled to the organic floor (which can be epithelial tissue or mucus coat at the floor of the tissue), in mucoadhesion the polymer is connected to the mucus floor (the substrate). Additionally, oral mucosal transport is divided into three categories:

(i) Buccal transport, management through the mucosal linings of the cheeks (buccal mucosa);
(ii) Sublingual transport, systemic transport of healing compounds through the mucosal floor of the mouth;
(iii) Neighborhood transport, management through the oral cavity.

Sublingual delivery is advantageous for the rapid initiation of healing motion (example: sublingual nitroglycerin for the treatment of Angina pectoris) and the buccal mucosa is generally relevant for drug management. There is a lot of interest in the mucoadhesion concept among the pharmaceutical industry and is effectively employed as a management direction. Mucoadhesive drug transport devices can be delivered in a variety of ways:-

- Buccal delivery mechanism
- Oral delivery system,
- Vaginal delivery system,
- Rectal delivery system,
- Nasal delivery system,
- Ocular delivery system

Mucoadhesive Drug Delivery System Routine.
- Buccal Delivery System: One option for oral drug administration, particularly for capsules that undergo first-by-skip, is buccal delivery of medication effect. The buccal mucosa's stratified squamous epithelium, which is maintained by the connective tissue known as the lamina propria, was previously targeted as a site for drug delivery.
- Oral Delivery System: Accordingly, it is thought that an oral drug delivery system will provide continuous oral release of the medication during the course of its gastrointestinal (GI) transit. Oral health is the most well-known despite the fact that it leads to more extremely difficult circumstances due to the engagement of the gastro-intestinal (GI) device and the drug bioavailability) direction for drug shipping. Lipid-based entirely oral shipping structures have been revised, and this research stresses the importance of each device's role in the performance of the shipping process.
- Vaginal Delivery System: For both systemic and local disorders, vaginal delivery is a crucial route of drug administration. An important component of medication treatment for both localized disorders and systemic diseases is vaginal delivery. There are certain advantages to the vaginal route because as a result of its enormous floor surface, abundant blood supply, avoidance of the first-by skip effect, and particularly significant permeability to numerous capsules and self-insertion.
- System for Rectal Delivery The management of medication or medications through the rectum for local or systemic effects is referred to as rectal drug delivery. A rectal medication shipping device is a type of mucosal adhesive drug delivery device. These buildings provide Using a potent carrier, the medication adheres to the mucosal membrane through mucoadhesion.
Ocular Delivery System: The eye is a complex organ with unique anatomical and physiological characteristics. The term "ODDS" refers to a novel medication delivery method that may be inserted into the conjunctival or cul-de-sac of the eye.

**Mucoadhesion mechanism**

The mucin layer of the mucosal tissue and one artificial material, such as mucoadhesive polymer, are held together by the interfacial force of attraction is referred to as mucoadhesion. The term "mucoadhesive" refers to an artificial material, Mucus membranes interact with them, staying on them, or holding them together for prolonged or extended time. There are two steps during the adhesion process that have been identified: as follows.

1. **Contact Phase**

2. **Stage of Consolidation**

![Fig no : mechanism of MDDS](image)

**Theories mucoadhesion:**

The **electronic theory**

Holds that changes in digital structure cause an electron switch to occur when a mucus glycoprotein community and a sticky polymer come into contact. It is thought that doing this will result in the construction of a digital double layer on the contact, with subsequent adhesion brought about by attractive forces present throughout the double layer.

The **theory of wetting**

It is mostly used with liquid systems and concerns floor and interfacial energy. It includes the capacity for a fluid to spread instantly over a surface as a necessary component for the formation of a bond.

**Adsorption Theory:**

According to this concept, the attachment of adhesive on the premise of hydrogen bonding and Vander Waals forces. Two kinds of chemical bonds including primary covalent & secondary chemical bonds (consisting of electrostatic forces, Vander Waals forces & hydrophobic bonds).

This is another widely accepted theory, where adhesion between the substrate and adhesive is due to primary and secondary bonding.

According to the Adsorption Theory, hydrogen bonds and Vander Waals forces are what hold adhesives together. Chemical bonds can be classified into two categories: primary covalent bonds and secondary chemical bonds (composed of electrostatic forces, Vander Waals forces, and water-repellent bonding). Another generally accepted theory states that primary and secondary bonding is responsible for the adherence between the substrate and adhesive.

The **Diffusion Theory**

States that when mucus and polymer chains combine well enough, a semi-permanent sticky bond is formed. This approach is limited by available molecular chain lengths and is driven by a concentration gradient their flexibility.

**Factor affecting on mucoadhesion:**

**Molecular Weight**: The mucoadhesive energy of a polymer increases with molecular weights above 100,000. Direct correlation between the mucoadhesive power of polyoxyethylene polymers and their molecular weights lies within the range of two hundred,000–7,000,000.

**Flexibility**: Mucoadhesion starts with the diffusion of the polymer chains in the interfacial region. Therefore, it is important that the polymer chains contain a substantial degree of flexibility in order to achieve the desired entanglement with the mucus. The increased chain inter penetration was attributed to the increased structural flexibility of the polymer upon incorporation of polyethylene glycol.
Pass-linking density: The common pore length, the number and common molecular weight of the pass-linked polymers, and the density of pass-linking are 3 essential and inter-associated structural parameters of a polymer network. Consequently, it appears reasonable that with increasing density of move-linking, diffusion of water into the polymer community happens at a lower fee which, in turn, causes an insufficient swelling of the polymer and a decreased fee of interpenetration between polymer and mucin.

Hydrogen bonding potential: Hydrogen bonding is every other essential component in mucoadhesion of a polymer. desired polymers need to have practical business which can be capable of form hydrogen bonds, and versatility of the polymer is vital to improve this hydrogen bonding capacity. Polymers including poly(vinylalcohol), hydroxylated methacrylate, and poly(methacrylic acid), in addition to all their copolymers, have suitable hydrogen bonding capacity.

Hydration: Hydration is needed for a mucoadhesive polymer to amplify and create a proper macromolecular mes of enough size, and also to result in mobility inside the polymer chains so as to enhance the interpenetration process among polymer and mucin. Polymer swelling lets in a mechanical entanglement by using exposing the bioadhesive sites for hydrogen bonding and/or electrostatic interaction between the polymer and the mucus community. but, a vital degree of hydration of the mucoadhesive polymer exists where premier swelling and mucoadhesion occurs.

concentration: The importance of this thing lies in the improvement of a strong adhesive bond with the mucus, and may be explained by using the polymer chain period available for penetration into the mucus layer. while the concentration of the polymer is too low, the quantity of penetrating polymer chains per unit quantity of the mucus is small and the interaction among polymer and mucus is risky. In popular, the more focused polymer might result in a longer penetrating chain period and higher adhesion. however, for every polymer, there may be a crucial awareness, above which the polymer produces an “unperturbed” nation due to a appreciably coiled shape. As a end result, the accessibility of the solvent to the polymer decreases, and chain penetration of the polymer is significantly decreased. there fore, better concentrations of polymers do no longer necessarily improve and, in a few instances, absolutely decrease mucoadhesive homes. one of the research addressing this issue confirmed that excessive concentrations of bendy polymeric films primarily based on polyvinylpyrrolidone or poly(vinyl alcohol) as film-forming polymers did not similarly decorate the mucoadhesive properties of the polymer.

Conclusion: The mucoadhesive dosage forms offer prolonged touch on the website online of administration, low enzymatic pastime, and affected person compliance. The method of mucoadhesive drug delivery device depends on the selection of suitable polymer with tremendous mucosal adhesive houses and biocompatibility. Now researchers are looking past conventional polymers, specially subsequent-technology mucoadhesive polymers (lectins, thiol, and so on.); these polymers offer greater attachment and retention of dosage paperwork. but, these novel mucoadhesive formulations require tons extra paintings, to supply clinically for the remedy of both topical and systemic sicknesses. The phenomenon of mucoadhesion may be used as a version for the controlled drug delivery procedures for a number of drug candidates. there may be no doubt that the oral path is the maximumfavoured and probably most complex direction of drug shipping. The buccal mucosa gives numerous advantages for managed drug delivery for extended intervals of time. The mucosa is nicely supplied with each vascular and lymphatic drainage and first-bypass metabolism inside the liver and pre-systemic elimination within the gastro.

Reference:


Adhikari SN, Nayak BS, Nayak AK, Mohanty B. Formulation and evaluation of buccal patches for delivery of atenolol. AAPS Pharmscitech. 2010 Sep 1;11(3):1038-44.


