MUCOADHESIVE DRUG DELIVERY SYSTEM

Mucoadhesive drug delivery system interact with the mucus layer covering the mucosal epithelial surface, & mucin molecules & increase the residence time of the dosage form at the site of the absorption. Mucoadhesive drug delivery system is a part of controlled delivery system.

ADVANTAGES-

- MDDS offer several advantages over other controlled oral controlled release systems by virtue of prolongation of residence of drug in GIT.
- Targeting & localization of the dosage form at a specific site.
- High drug flux at the absorbing tissue.
- MDDS will serve both the purposes of sustain release & presence of dosage form at the site of absorption.
- Excellent accessibility.
- Painless administration.
- Low enzymatic activity & avoid of first pass metabolism.

DISADVANNTAGES-

- If MDDS are adhere too tightly, it is undesirable to exert too much force to remove the formulation after use, otherwise the mucosa could be injured.
- Some patient suffers unpleasent feeling.
- Unfortunately, the lack of standardized techniques often leads to unclear results.
- Costly drug delivery system.
- Medications administered orally do not enter the blood stream immediately after passage through the buccal mucosa.

MECHANISMS OF MUCOADHESION

The mechanism of adhesion of certain macromolecules to the surface of a mucous tissue is not well understood yet. The mucoadhesive must spread over the substrate to initiate close contact and increase surface contact, promoting the diffusion of its chains within the mucus. Attraction and repulsion forces arise and for a mucoadhesive to be successful, the attraction forces must dominate. Each step can be facilitated by the nature of the dosage form and how it is

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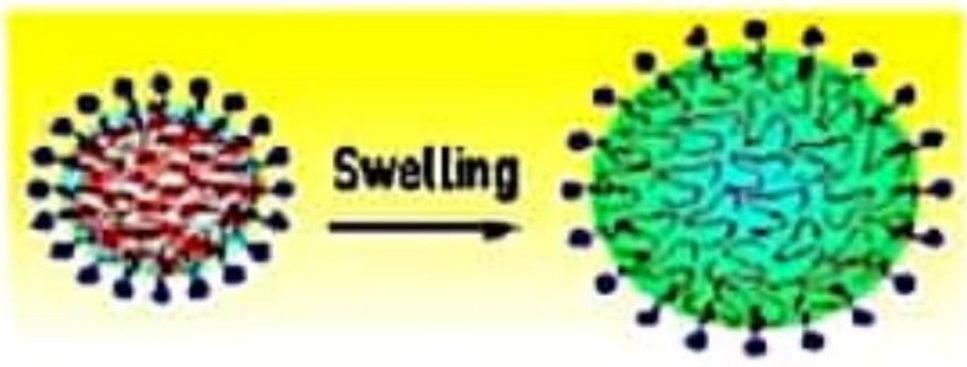
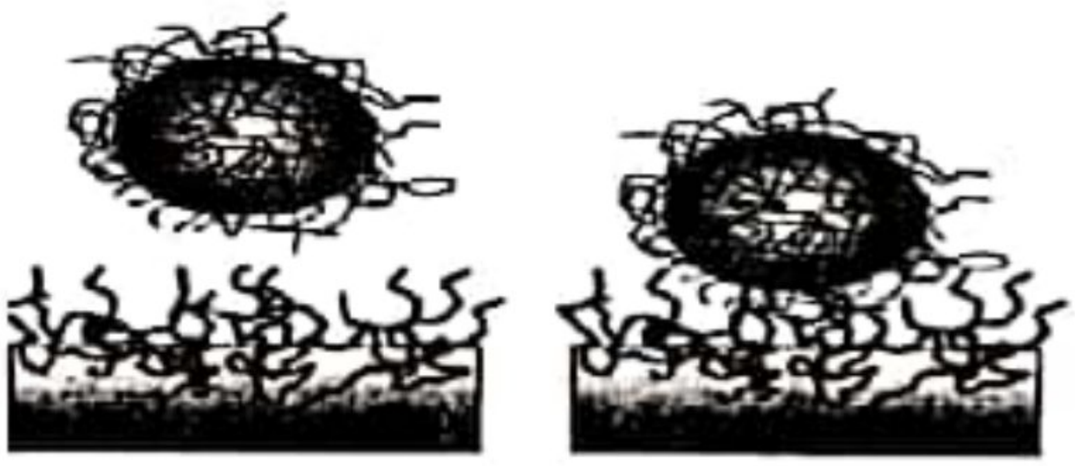
administered. For example, a partially hydrated polymer can be adsorbed by the substrate because of the attraction by the surface water. Thus, the mechanism of mucoadhesion is generally divided in three steps,

Step-I: The first stage is characterized by the contact between the mucoadhesive and the mucous membrane, with spreading and swelling of the formulation, initiating its deep contact with the mucus layer. In some cases, such as for ocular or vaginal formulations, the delivery system is mechanically attached over the membrane. On the other hand, in the gastrointestinal tract direct formulation attachment over the mucous membrane is not feasible. Peristaltic motions can contribute to this contact, but there is little evidence in the literature showing appropriate adhesion.

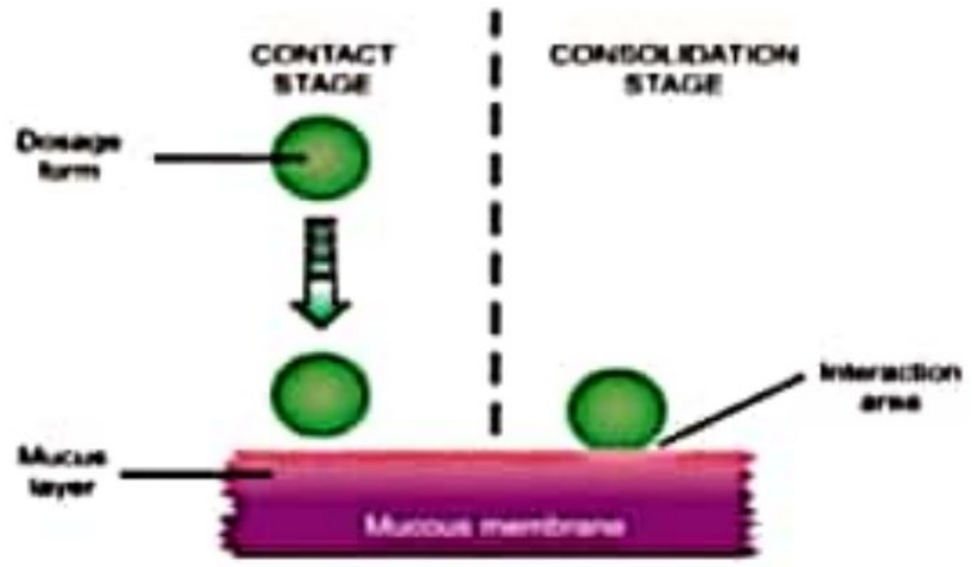


Step-II: In this step the mucoadhesive polymer chain and the mucosal polymer chains intermingle and entangle to form adhesive bonds strength of bonds depends upon the degree of penetration of the two polymer groups.



Step-III: This step involves formation of weak chemical bonds between the entangled polymer

chains. Bonds include primary bonds such as covalent bonds and secondary interactions such as vanderWaals and hydrogen bonds.



MUCOADHESION THEORIES

Various theories exist to explain at least some of the experimental observations made during the bioadhesion process. However five main theories can be distinguish.

- Wetting theory
- Electronic theory
- Fracture theory
- Adsorption theory
- Diffusion theory

Wetting theory

The wetting theory applies to liquid systems which present affinity to the surface in order to spread over it. This affinity can be found by using measuring techniques such as the contact angle. The general rule states that the lower the contact angle then the greater the affinity. The contact angle should be equal or close to zero to provide adequate spreadability.

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.

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. For example, hydrogen bonds are the prevalent interfacial forces in polymers containing carboxyl groups. Such forces have been considered the most important in the adhesive interaction phenomenon because, although they are individually weak, a great number of interactions can result in an intense global adhesion.

Fracture theory

This theory describes the force required for the separation of two surfaces after adhesion. The fracture strength is equivalent adhesive strength through the following equation. This theory is useful for the study of bioadhesion by tensile apparatus.

$$\sigma = (E \times \varepsilon/L)^{1/2}$$

where σ is the fracture strength, ε is fracture energy, E young modulus of elasticity and L the critical crack length.

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.[15] This penetration rate depends on the diffusion coefficient, flexibility and nature of the mucoadhesive chains, mobility and contact time. According to the literature, the depth of interpenetration required to produce an efficient bioadhesive bond lies in the range 0.2-0.5 μm.

This interpenetration depth of polymer and mucin chains can be estimated by equation.

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

where t is the contact time and D_3 is the diffusion coefficient of the mucoadhesive material in the mucus.

Mechanical theory

Mechanical theory considers adhesion to be due to the filling of the irregularities on a rough surface by a mucoadhesive liquid. Moreover, such roughness increases the interfacial area available to interactions thereby aiding dissipating energy and can be considered the most important phenomenon of the process. It is unlikely that the mucoadhesion process is the same for all cases and therefore it cannot be described by a single theory. In fact, all theories are relevant to identify the important process variables.

FACTORS AFFECTING MUCOADHESION

Polymer related factors

Molecular weight

Mucoadhesive pr of the polymer increases with increase in molecular weight of polymeric chain.

Chain length

As chain length of the polymeric materials increases mucoadhessiveness also increases.

Spatial arrangement

Along with different material related factors (weight and length of polymer) spatial arrangements or conformation of a molecule is another necessary factor for mucoadhesive property. A very good example for this is dextran in which helical structure of dextran may enclose many active groups of adhesive property, unlike poly ethylene glycol polymer which possess a linear structural confirmation.

Flexibility

Flexible nature of polymer is another important parameter for mucoadhesive property because chain length of polymer facilitates good penetration and attachment of the polymer chains with mucosal lining of the biological membrane and helps in improvement of bioadhesive property. The flexibility of the polymer chains is generally affected by hydration and cross linking reactions of the polymer network.

Hydration of polymer

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