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Review Article

Review: A Mucoadhesive drug delivery system

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ABSTRACT

The drug action can be improved by developing the new drug delivery system, such as the mucoadhesive drug delivery system. These systems remain in close contact with absorption tissue the mucus membrane, releasing the drug action site leading to a bioavailability rise and both local and systemic effect . The mucoadhesion is currently explained by 5 theories: Wetting, Electrostatic, Diffusion, Adsorption, Fracture. The polymers used for the formulation of mucoadhesive drug delivery system are PAA (polyacrylamide acid),chitosan, collagen, gelatin and newer second-generation polymers. The process of complex one that includes process such as wetting, adsorption and interpretation of polymer chain. The mucoadhesive ability of a dosage form is depend upon the variety of factors, including the nature of the mucosal tissue and the physicochemical properties of the polymeric formulation. Mucoadhesive system have found wide use throughout many mucosal covered organelles for active ingredients delivery for local or systemic effect. The administration of the drug by the buccal route has several advantages over per oral administration such as quick action improved the patient compliance particularly with the paediatrics and geriatric patient. It includes detail information about mucus, advantages, disadvantages of drug delivery system, mechanism , factors affecting on mucoadhesive drug delivery, mucoadhesive dosage form, mucoadhesive polymer and application of mucoadhesive drug delivery system.

INTRODUCTION

"Since the early 1980s, the concept of mucoadhesion has gained considerable interest in pharmaceutical technology. Adhesion can be defined as the bond produced by contact between a pressure sensitive adhesive and a surface. The American Society of Testing and Materials has defined it as the state in which two surfaces are held together by interfacial forces, which may consist of valence forces, interlocking action or both. Mucoadhesive drug delivery systems prolong the residence time of the dosage form at the site of application or absorption. They facilitate an intimate contact of the dosage form with the underlying absorption surface and thus improve the therapeutic performance of the drug. In recent

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years, many such mucoadhesive drug delivery systems have been developed for oral, buccal, nasal, rectal and vaginal routes for both systemic and local effects. Bioadhesion is defined as an ability of a material to adhere to a biological tissue for an extended period of time.

Bio adhesion can be classified into 3 types,

Type 1: Adhesion between two biological phases. Example platelet aggregation and wound healing.

Type -2: Adhesion of a biological phase to an artificial substrate. Example cell adhesion to culture dishes and biofilm formation on prosthetic devices and insert.

Type-3: Adhesion of an artificial material to a biological substrate, for example, adhesion of synthetic hydrogels to soft tissues and adhesion of sealants to dental enamel.

The mucosal route of drug delivery is

1. Buccal\Oral route
2. Nasal route
3. Ocular route / Opthalmic drug delivery system
4. Vaginal route / Rectal drug delivery system
5. GIT route.

Advantages Of Mucoadhesive Drug Delivery System:

1. Better patient compliance
2. Lower dose frequency
3. It avoids the first pass metabolism
4. Excellent accessibility as well as rapid onset of action possible
5. Not only rapid healing but also cellular recovery of the local site
6. Drug is protected from degradation in the acidic environment in the GIT
7. Shorter treatment period
8. Increased safety margin of high potency drugs due to better control of plasma levels.

Disadvantages Of Mucoadhesive Drug Delivery System:

1. In case of ocular formulation, the formulation / medicament may cause uneasiness as well as blurring.
2. Eating and drinking is prohibited.
3. The vaginal formulation may be contraindicated in case of pregnancy
4. The formulation may irritate the sensitive nasal mucosa.
5. The dosage form given by any route may get dislodged from his position
6. Occurrence of local ulcerous effects due to prolonged contact of the drug possessing ulcerogenic property.
7. 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.

Theories Of Mucoadhesion / Bonding Mechanism:

A complex process and numerous theories have been proposed to explain the mechanism involved in Mucoadhesion. There are six general theories which have resulted from studies on the performance of variety of material and polymer- polymer adherence. The process of mucoadhesion is mainly based on formation of two kind of bond between bio adhesive and system and mucus membrane.

They are:

Chemical bond :

It may include into the covalent bonds, weak secondary bonds, ionic bond and hydrogen bond etc.

Mechanical bond :

The mechanism bond can be arising from the physical connection between two surfaces. It is same to that interlocking system.

1. Wetting Theory :

This theory is based on mechanism of spreadabillity drug dosage form across the biological layer. This theory applies to liquid systems Which is the affinity of a liquid to maintain contact

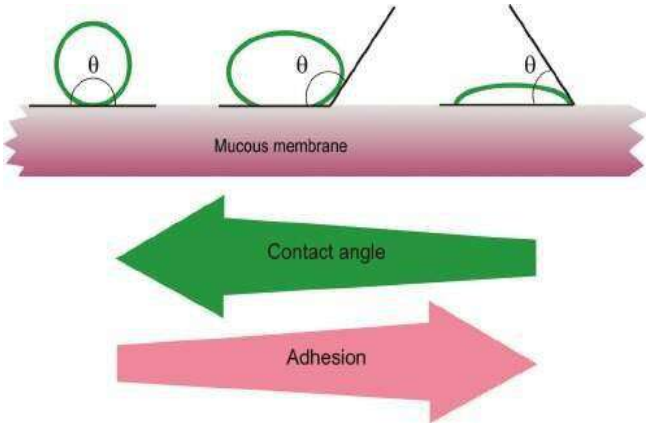

Fig no 1: Influence of contact angle between device and mucus membrane on bioadhesion.

in the surface. The affinity between the liquid systems and the mucous membrane is obtained by asserting the contact angle. As a basic concept, As the contact angle decreases the affinity increases. The contact angle must be near zero to provide sufficient spreadability.

2. Diffusion Theory / Diffusion Interlocking Theory:

Diffusion theory is chain entanglement between glycoproteins of the mucus and the mucoadhesive polymer to create a semi-permanent adhesive bond. The bond strength increases with increase in the degree of penetration. This penetration rate depends on the diffusion coefficient, flexibility and nature of the mucoadhesive chain, mobility and contact time. Sufficient depth of penetration creates a semi – permanent adhesive bond. The depth of interpretation required to produce a firm bio adhesive bond lies in the range 0.2 - 0.5 um. The typical value of the polymer diffusion coefficient through the glycol protein network of the mucous may be in the range of 10-10 to 10-16 cm2per second. The interpenetration depth of polymer and Mucin chains can be is estimated by the following equation:

The interpenetration death

$$I = (t\ Db)1/2$$

Where,

t = contact time

Db = diffusion coefficient of the mucoadhesive material in the mucus.

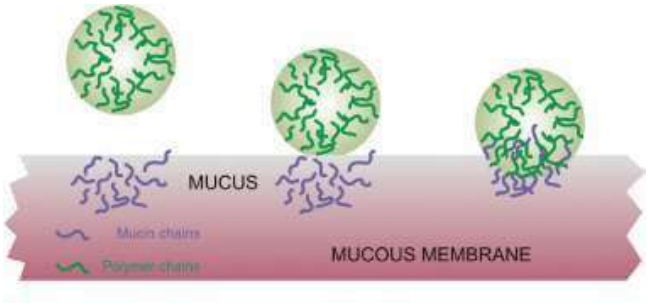

Fig no 2: Secondary interaction resulting from interdiffusion of polymer chains of bioadhesive device and mucus.

In order for diffusion to occur. It is important that the components involved have good mutual solubility that is the both bioadhesive and the mucus have similar chemical structures. The greater the structural similarity, the better is the mucoadhesive bond.

3. The Fracture Theory:

This is most utilized theory in studies on the mechanical estimation of mucoadhesion. Differs small from the other five in that it relates the adhesive strength to the forces required for the detachment of the two involved surface after adhesion. The Fracture Theory is mainly based on the fact that, the forces required to detach the polymeric chain from the mucin layer is the strength of their adhesive forces. This strength may be also called as fracture strength. The fracture strength can be determined by using the formula given below:

$$G = (E.e/L)1/2$$

Where,

G = Fracture strength

E = Young's modules of electricity

e = Fracture energy

L = Critical crack length.

The force Sm is frequently calculated in tests of resistance to rupture by the ratio of

the maximum detachment force fm and the total surface area Ao involved in the

adhesive interaction.

$$Sm = Fm / Ao$$

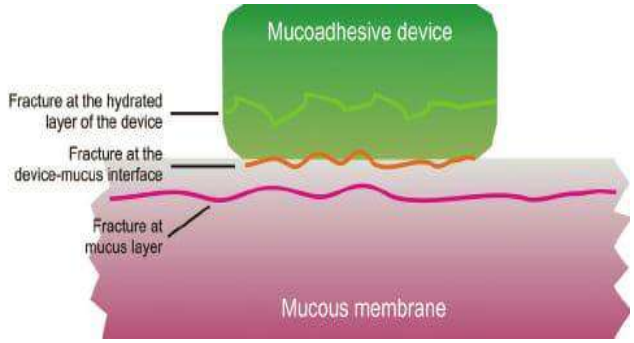

Figure no 3:Region of Mucoadhesive bond rupture can occur.

4. Mechanical Theory:

Mechanical theory considers adhesion to be due to the filling of the irregularities on a rough region by a mucoadhesive liquid Moreover, such scratch rise. The interfacial Area available to interactions there by aiding dissipating energy and can be considered the most basic phenomenon of the process. It is unlikely that the mucoadhesion process is the same for all cases and therefore it cannot be explained by a one or single theory. In fact, all theories are relevant to identify the important process variables. The mechanism governing 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, chain flexibility, for linear polymer mucoadhesion rice with molecular weight but the same relationship doesn't join for non-liner polymer. After application search steam trade easily, since they present rheological properties of a liquid but gelify as they come into contact the adsorption site thus preventing their rapid removal.

5. Electronic Theory / Electrostatic Theory:

Electronic theory describes adhesion as a phenomenon in which there occurs electron transfer between the mucus and the mucoadhesive system as a result of the differences in their electronic structures. This electron leads to a formation of double layer of electric charge at the mucus and the mucoadhesive interface. The result of this is the formation of attractive forces within this double layer. There is controversy over the acceptance of this theory due to the fact it explains the electrostatic force, which are much weaker as the causes of bond adhesion. The bio adhesive force is believed to be present.

6. Adsorption Theory:

Adsorption Theory States that the bio adhesive bond formed between an adhesive substrate and the tissue is due to the weak Van Der Waals force and hydrogen bond formation. Various mucoadhesive interaction are :

a Ionic bonding
b Covalent bonding
c Hydrogen bonding
d Van Der Waals interactions
e Hydrophobic bonding.

For example- Hydrogen bond are the prevalent interfacial forces in polymer containing carboxyl group such forces have been considered the most important in the adhesive interacts can result in an intense global adhesion. The adhesion is defined as a result of several interaction between two surface these theories describe the involvement of two kind of chemical bond.

A. Primary bond :

Ionic chemicals, covalent and metallic unions, which are not desired because they are permanent.

B. Secondary bond :

Van Der Waals forces, hydrophobic interactions and hydrogen bonds required less energy and the most interaction in mucoadhesion.

Mucoadhesive Dosage form:

a. Tablet or mucoadhesive tables
b. Patches
c. Films / wafers
d. Gel and ointment
e. Spray
f. Pastes
g. Lozenges
h. Chewing gum

1. Tablets or Mucoadhesive Tablet:

Unlike traditional table, mucoadhesive tables can be used on the buccal or sublingual or Oral to allow quick onset of action and controlled drug delivery through rise gastric retention time of the dosage form. They adhere to the mucosa and remain held in position till release is complete. Mucoadhesive tablets provide efficient absorption and better bioavailability of the drug because of a large surface to volume ratio and promote much closer connection with the mucus layer. Tablets are small flat as well as oval with a diameter of approximately 5-8 mm.

2. Patches:

There are different types of oro – adhesive patches:

a Patches with a dissolvable matrix for drug delivery to the oral cavity:

These patches are longer acting then solid forms such as tablet and lozenges and can produce sustained drug release for treating oral candidiasis and mucositis. They slow and completely dissolved during use leaving nothing to remove.

b Non dissolvable backing patches system:

These are for Systemic drug delivery of drug and they after protection from saliva. The patches deliver a concentrated does of the drug into the oral mucosa for 10-15 hours.

3. Wafers / films:

Mucoadhesive films may be preferred over adhesive tablet in term of flexibility and comfort. In addition, they can circumvent the relatively short residence time oral gel on the mucosa which are easy washed away and removed by saliva. An ideal film should be flexible elastic and soft it adequately strong to with stand breakage due to praise from mouth movement. Thin strip of polymeric film, capsule, loading up to 20 mg of drugs dissolve on the tongue in less than 30s and deliver drug directly to the blood supply for rapid treatment of condition such as important, pain relief, migraines, nausea and motion sickness.

4. Gels and Ointment:

Semisolid dosage form, such as gels and ointment, have the advantages of easy dispersion throughout the oral mucus Gels are used for localized action in a site-specific manner. The application of mucoadhesive gels provides an extended retention time in the oral cavity adequate drug penetration as well as high efficacy and patient acceptability. A major application of adhesive gel in the local delivery of medicinal agents for the treatment of periodontitis which is an inflammatory and infectious disease that causes formation of pockets between the gum and the tooth and can eventually causes loss of teeth. HPMC has been used as an adhesive ointment ingredient. Additionally, a highly viscous gel was developed from Carbopol and hydroxypropyl cellulose for ointment dosage form that could be e maintained on the tissue for up to 8 hours.

5. Spray:

The viscosity and size of the droplets are monitored in order to ensure delivery to the oral cavity rather than to the lungs. They are capable of delivering large molecules such as insulin across the oral mucosa. The generex biotechnology corporation has developed a rapid mist spray which is capable of delivering large molecules such as insulin across the oral mucosa.

6. Pastes:

Utilised pastes for in the delivery of antimicrobial agent for improved extraction socket healing after the tooth extraction in patient with HIV disease and for the delivery of controlled release triclosan in oral care formulations. Mucoadhesive pastes with methylprednisolone hydrogen succinate have been characterized with carbomer polymer.

7. Lozenges:

lozenges can be used as a alternative dosage form to tablet and capsules when patients are unable to swallow. The use of lozenges has been reported for systemic drug delivery but it is more usual to see

this dosage form used to the oral cavity or the throat area.

8. Chewing gum:

Gums are now considered pharmaceutical dosage forms and have been used to deliver drug for buccal absorption. This formulation consists of a gum bas which primarily consists of resins. Elastomer, waxes and fats. Additives such as sweetener, glycerol and flavors can be added as desired. These chewing gum move about in the oral cavity and the process of chewing mix it with the saliva where the process drug is fast dissolved, partitioned and then absorbed into the mucosal membrane. Thus, solubility of the drug in saliva is an important factor in increasing the amount of drug release and absorbed.

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