MUCOSAL DRUG DELIVERY SYSTEM

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Introduction-

Mucosa is most of some organ and body cavity such as nose, mouth, lungs, stomach. It is alternative method of systemic drug delivery. It is interact with mucus layer covering mucosal layer epithelial surface and mucin molecule. Adhesion can produce by contact between pressure sensitive adhesive & surface. mucoadhesive drug delivery system interact with mucosa layer covering the mucosal epithelial surface and main molecules &increases the recidence time of the dosage form at the site of absorption . Muco adhesive DDS is a part of control delivery system. Since the early 1987 the concept of the mucosa adhesion has gained consider interest in the pharmaceutical technology. Combine muco adhesive with enzymes inhibitory and penetration enhancer properties and improve the patient compliance. Hydrophilic high molecular weight such as peptide that cannot be administered and poor absorption then MDDS is best choice

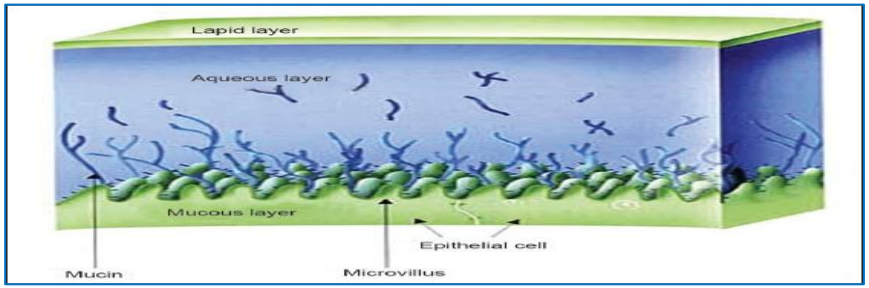


Fig.no.1 Mucosal drug delivery system

Concept-

- Chemical bond- covalent bond, weak secondary bond, ionic bond, hydrogen bond.
- Mechanical bond-the physical connection between two surfaces. Similar interlock system

- **Bio-adhesion-**
- Principle- Bio-adhesion includes cell-to-cell adhesion, bacteria, binding to surface adhesion to mucus membrane & the use of adhesive material in medical treatment

Mechanism-

- Step 1-wetting and swelling of polymer.
- Step 2- interpenetration between the polymer change & mucosal membrane Step
- Step 3 -consolidation stage

Step 1-wetting and swelling of polymer

The wetting and swelling step occurs when the polymer spread over the surface of the biological substrate or mucosal membrane in order to develop an intimate contact with the substrate. This can be readily achieved for example by placing a mucoadhesive formulation such as tablet or paste within the oral cavity vagina .swelling of polymer occur the because the component within the polymers have affinity for water

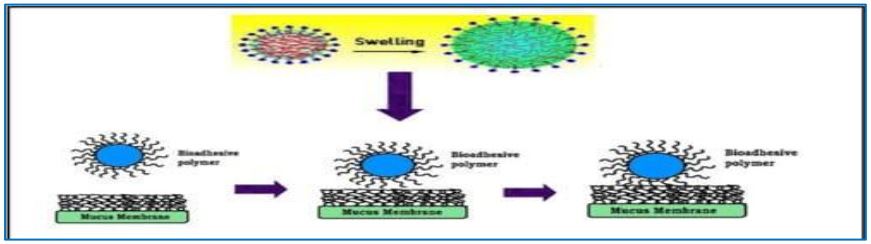


Fig.no.2 swelling of polymer

Step 2- interpenetration between the polymer change & mucosal membrane Step

The surface of mucosal membrane are composed of high molecular weight polymer known as glycoproteins. In step 2 of mucoadhesive bond formation the mucoadhesive polymer chain and mucosal polymer chains intermingle and entangle to form permeable adhesive bonds. The strength of these bond depends on degree of penetration between to polymer groups. in order to strong adhesive bond , one polymer group must be soluable in other and both polymer type must be of similar chemical structure

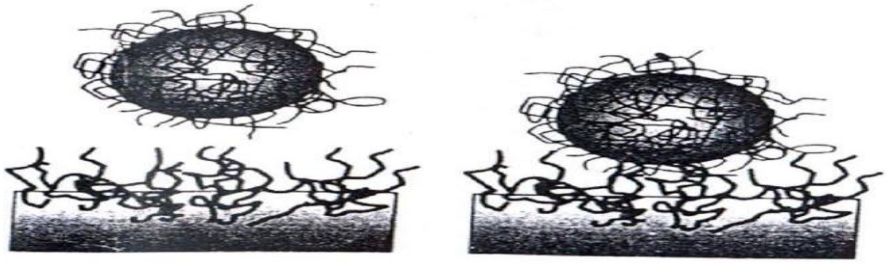


Fig.no.3 interpenetration between the polymer change & mucosal membrane Step

Step 3 -consolidation stage

This steps involve the formation of weak chemical bond between the entagled polymer chains. The type of bonding formed betwwen the chains include primary bond such as the covelent bond s and weaker secondary interaction such as van der wall interactions and hydrogen bonds. Both primary and secondary bonds are exploited I manufacture of mucoadhesive formulations in which strong adhesives between polymers are formed

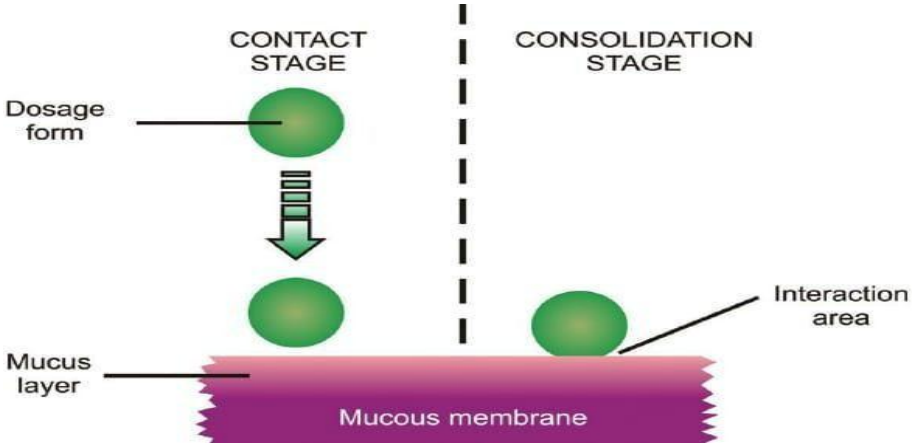
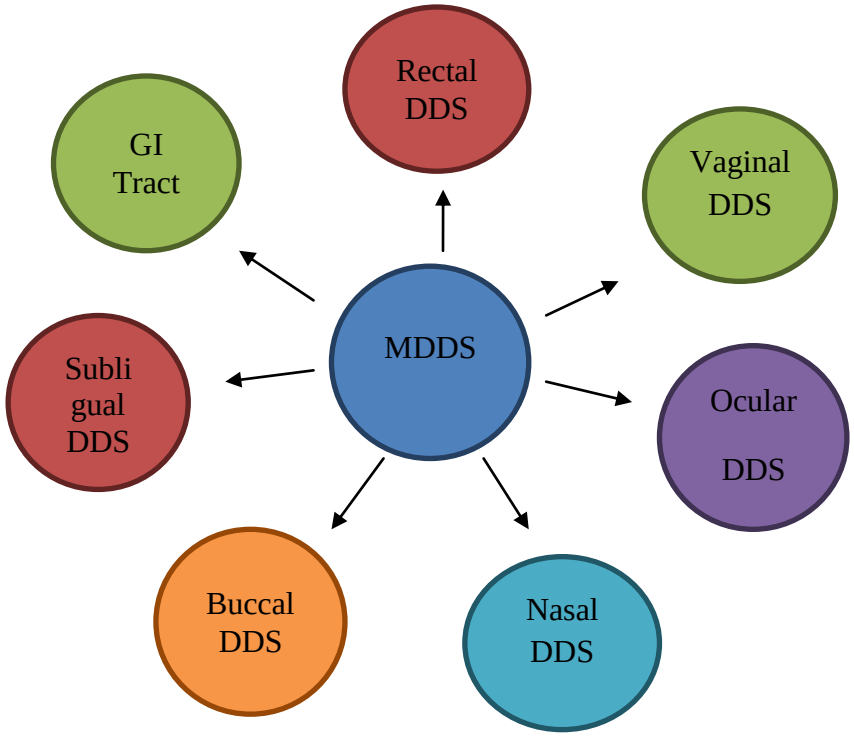
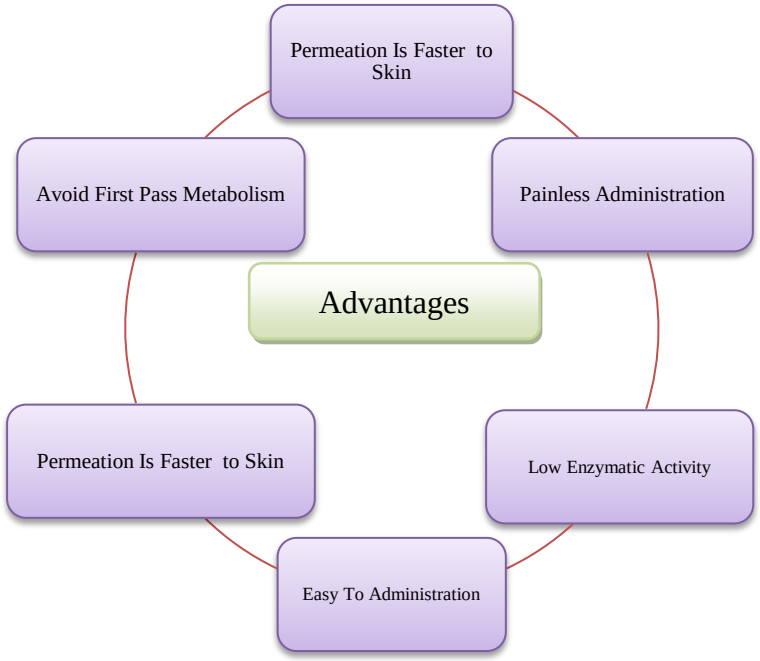
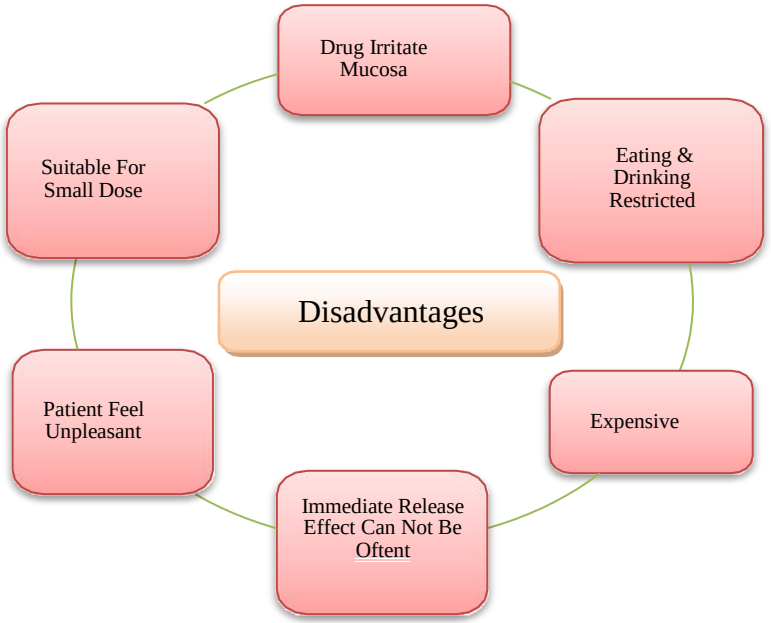


Fig.no.4 stages of consolidation

Different Routes Of Targeting MDDS:-







Trans mucosal permeability -

Mechanism: Two route involve in drug permeation across epithelial membrane

Para cellular route: Transfer of substance across an intracellular epithelium through Space bel cells.

Transcellular route: Cross the skin by directly pass through both the lipid Structure of intracellular region and moving across between the cells.

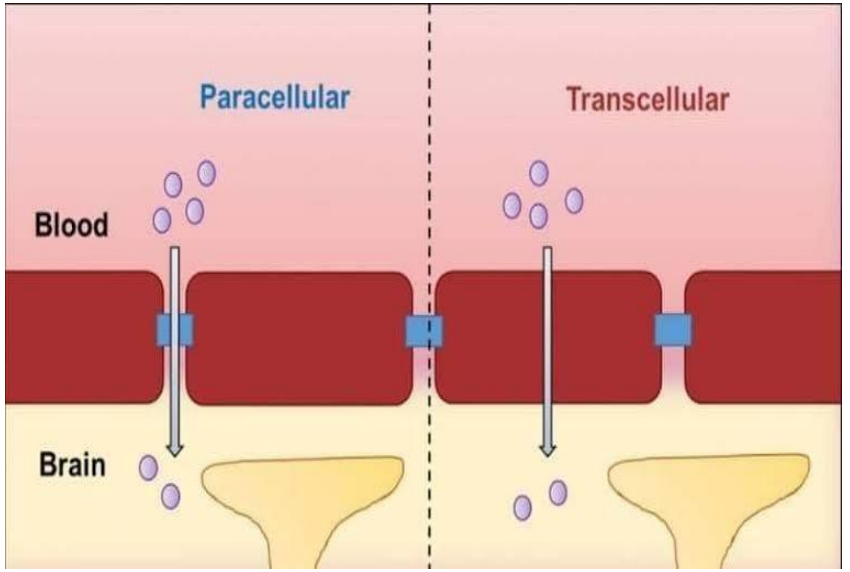


Fig.no.5 Tran's mucosal permeability

Factors of Trans mucosal Permeability:

Buccal drug delivery systems

1. Molecular size-

Small drug molecular 75-100 Dalton. The mucoadheshive strength of a polymer increase mol. Wt above 1,00,000

2. Lipid solubility-

More lipid soluble higher it's permeability

3. Degree of ionisation-

Non ionised form of drug have greater transport

4. Flexibility-

It Mucoadheshive starts with diffusion of polymer chains in interfacial region. Therefore is important that polymer chain contains a sustained degree of flexibility in order to achieve the desired entanglement with mucus

5. Cross linking density-

With increased density of cross linking diffusion of water into the polymer network occurs at a lower rate which in turn cause an insufficient swelling of the polymer and degree rate of interpretation between polymer and mucins

6. Lipophilicity of drug-

The permeability is higher for agent or drug that are highly lipid soluble salivary secretion higher the salivary secretion the higher the drugs chance of being flushed out. This can lead to incomplete absorption of the drugs

Drug may across cell membrane by:

1) Passive diffusion.

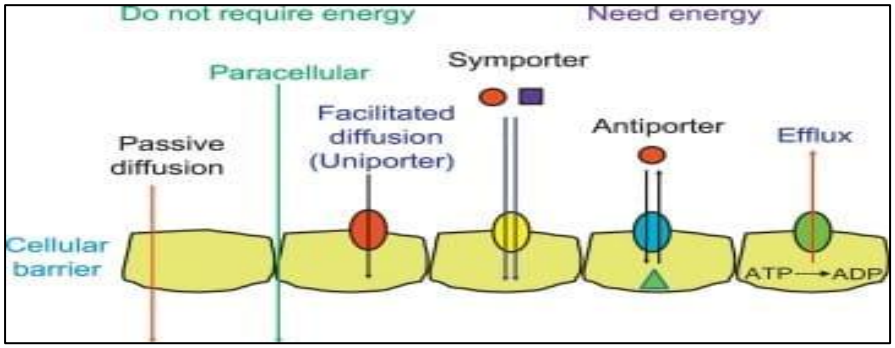
2) Facilitated diffusion.

3) Active transport.

4) Pinocytosis

Passive diffusion:-

Passive transport is the membrane transport that does not require energy to move substance across cell membrane. Instead of using cellular energy, like active transport, passive transport relies on the second law of thermodynamics to drive a movement of substance across cell membrane



Facilitated diffusion:-

In biology the passive movement of molecules or ions across the plasma membrane by means of a transport proteins located in the plasma membrane

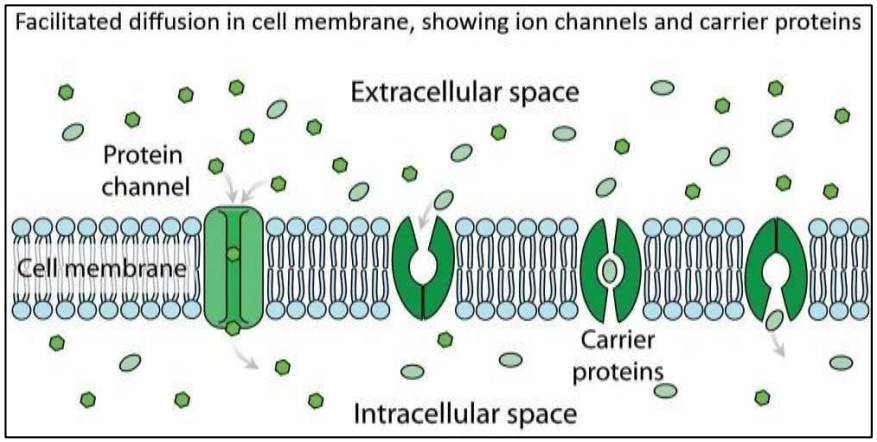


Fig.no.6 passive and facilitated diffusion

Active transport:-

Molecule move across cell membrane by two major processes diffusion or active transport .diffusion is the movement from a high concentration of molecule to low concentration of molecule moving molecule with cell energy is called active transport.

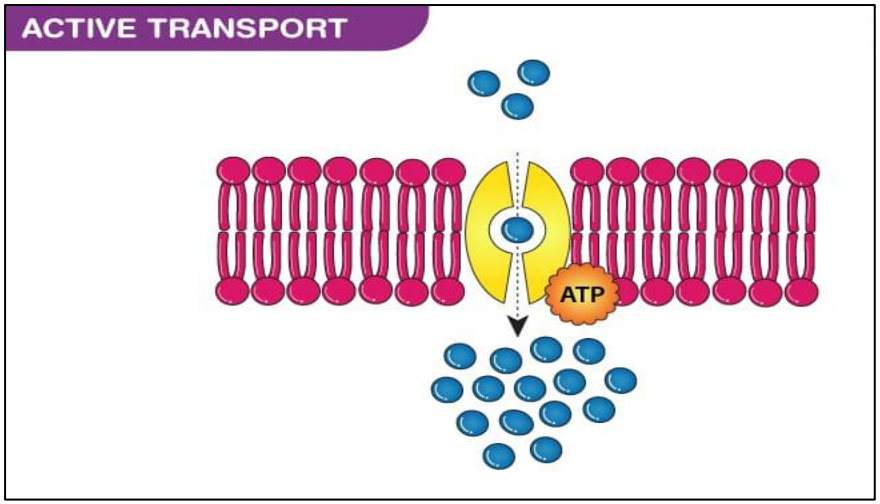


Fig.no.7 active transport

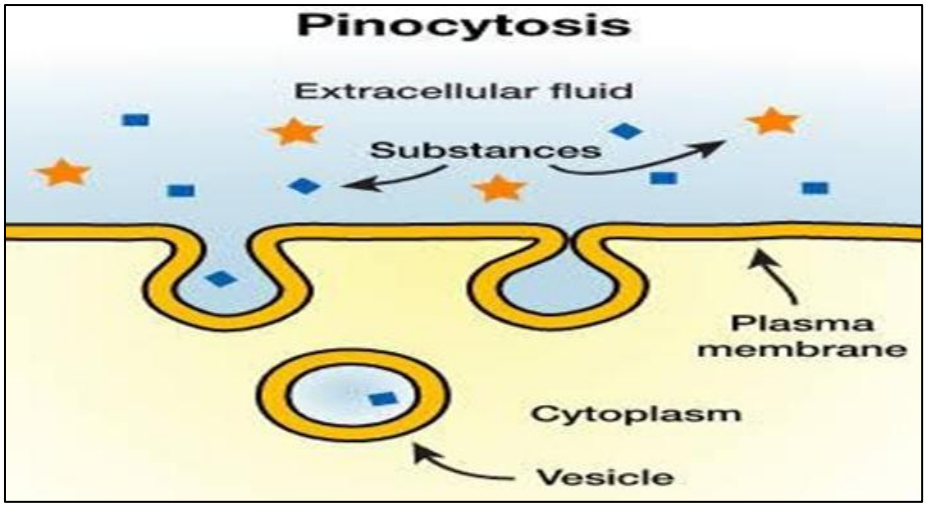
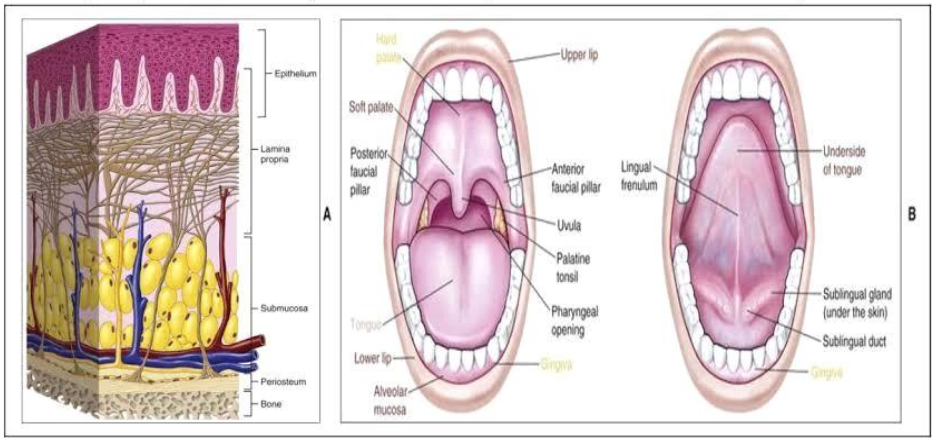


Fig.no.8 pinocytosis

Pinocytosis:-

Pinocytosis is the one type of endocytosis ,in general process by which cell engulf external substances gathering form into special membrane bound vesicle may carry within the cell it is believed that a vesical may carry extracellular fluid to the opposite side of the cell ,where it undergoes exocytosis.

Formulation consideration:-



Basic components:-

1. Drug substance-

Anionic polymer use in mucoadhesive polymerin pharmaceutical formulation. Eg. Poly acrylic acids

2. Bio- adhesive polymer-

Inert and compatible with environment. Natural polymers, eg- gelatin Synthetic and semisynthetic polymer, Eg-PVA, PEG

3. Backing membrane:-

It's also protects other layer and act as mechanical support. The backing layer control the Direction of release and reduce drug lose from the site of contact, Eg- PVA, ethyl cellulose

4. Permeation enhancer:-

Change mucosal rheology. Increased thermodynamic activities of drug, Egg- citric acid increased the fluidity of lipid bilayer membrane acting on compound at right junction

Marketed product-

A. Mucus-DM tablet,
B. Bio matrix capsules,
C. Macoupin gel

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