IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

REVIEW ON MUCOSAL DRUG DELIVERY SYSTEM

Dr. Ashish B. Navghare[1], Ravindra A. Sarkate[2], Gajanan N. Kawarkhe[3], Dr. Nandu Kayande[4], Priti B. Shinde[5]

[1]Department of QAT, Dr. R. N. Lahoti Institute of Pharmaceutical Education and Research center, Sultanpur, Buldana, India

[2]Department of Pharmaceutics, Dr. R. N. Lahoti Institute of Pharmaceutical Education and Research center, Sultanpur, Buldana, India

[3]Department of Pharmaceutics, Dr. R. N. Lahoti Institute of Pharmacy, Sultanpur, Buldana, India

[4]Department of Pharmacology, Dr. R. N. Lahoti Institute of Pharmaceutical Education and Research center, Sultanpur, Buldana, India

[5]Department of Pharmaceutics, Delight College of Pharmacy, Pune, India

ABSTRACT:

The primary goal of any drug delivery system is to administer the medication within a predetermined timeframe and to ensure that a therapeutic dose reaches the intended site of action. Mucoadhesive drug delivery represents a significant advancement in drug delivery systems. These dosage forms are designed to extend the duration of drug contact with mucosal surfaces, leading to benefits such as prolonged residence time, rapid onset of action, enhanced bioavailability, avoidance of hepatic first-pass metabolism, and controlled drug release rates. Mucoadhesive drug delivery can be employed through various routes including buccal, oral, nasal, ocular, gastrointestinal, vaginal, and rectal routes. In this system, the drug adheres to the mucosal epithelial surface upon contact with the mucous layer, facilitated by interfacial forces. Mucoadhesion refers to the mechanism by which two materials are bound together for a specific duration via attractive forces between biological materials and mucous membranes. This review article comprehensively discusses mucoadhesion, encompassing various theories, mechanisms, factors influencing, evaluations, and different forms of mucoadhesive dosage.

KEY WORDS: Mucoadhesive, Oral Mucosa, Bioadhesive. Factors and Evaluations

I. INTRODUCTION:

To produce a systemic pharmacological effect, various routes of drug administration are available. One common method is oral administration, where the drug is ingested and absorbed through the small intestine membrane, allowing it to enter systemic circulation. Consequently, oral administration is pivotal for achieving systemic effects. Conversely, the parenteral route is not typically utilized for self-administration of medication. Approximately 90% of systemic effect-inducing drugs are orally administered. Historical evidence suggests that drug solutes administered through buccal and sublingual routes are rapidly absorbed

into the reticulated vein located beneath the oral mucosa. Subsequently, they traverse through facial veins, the internal jugular vein, and the brachiocephalic vein, eventually reaching systemic circulation. Thus, buccal and sublingual administration routes offer a means of bypassing hepatic first-pass drug elimination. Among these routes, the buccal region within the oral mucosal cavity stands out as particularly significant for delivering drugs to systemic circulation. This is due to the rich blood supply and relatively permeable nature of the oral mucosa, coupled with the absence of Langerhans cells, which renders it tolerant to potential allergens.

Ideal Properties of Mucosal Drug Delivery System:

- Adherence to the attachment site for a few hours is desirable.
- Controlled release of the drug is necessary.
- Drug release towards the mucosa in a unidirectional manner is preferred.
- Facilitation of the rate and extent of drug absorption is important.
- Avoidance of irritation or inconvenience to the patient is crucial.
- Non-interference with normal functions, such as talking and drinking, is essential.

Mucosal drug delivery offers several advantages including:

- Medications can be easily administered, aiding in emergency situations where swift treatment is crucial.
- Medications are designed to release gradually over an extended period, ensuring sustained therapeutic effects.
- Medications can be given to patients who are unconscious or have suffered trauma, facilitating treatment in critical conditions.
- The utilization of drugs enhances their bioavailability as they bypass first-pass metabolism.
- Medications that are sensitive to the acidic environment of the stomach can be safely administered.
- Drugs are absorbed through passive diffusion mechanisms.
- Medications come into direct contact with the absorbing membrane, maximizing their absorption rate.
- The onset of drug action is rapid, leading to quick therapeutic effects.

Disadvantages:

- Drugs unstable at buccal pH cannot be administered.
- Drugs having a bitter or unpleasant taste, obnoxious odour, or those which irritate the mucosa cannot be administered.
- Drugs required in small doses can only be administered.
- Drugs absorbed by passive diffusion can only be administered.
- Eating and drinking may become restricted.

II. PRINCIPLES AND CONCEPTS OF BIOADHESION/MUCOADHESION

The concept of mucosal adhesives/ mucoadhesives was introduced in controlled drug delivery area in the early 1980s. It is the ability of synthetic or biological materials to adhere to a biological tissue for a prolonged time period. For drug delivery purposes, the term bioadhesion refers to the attachment of a drug carrier to a specific biological system. The term mucoadhesion refers to the adherence of drug to a mucus coat. Mucoadhesive drug delivery provides a close prolonged contact between the drugs and absorbing tissues, i.e., ocular, nasal, buccal, vaginal, GIT, and rectal.

Principles of Bioadhesion In conventional chemistry, it is believed that for adhesion the molecules should bind across the interface through the following bonds:

1) Ionic Bonds:

These strong bonds are formed when two oppositely charged ions attract each other through electrostatic interactions (e.g., in a salt crystal).

2) Covalent Bonds:

These strong bonds are formed when electron pairs are shared between the bonded atoms to fill the orbitals in both.

3) Hydrogen Bonds:

These bonds are generally weaker than ionic or covalent bonds. Hydrogen atom is slightly positively charged, thus is attracted to and covalently binds to electronegative atoms (such as oxygen or nitrogen).

4) Van der Waals Bonds:

These are some of the weaker forms of interaction. They arise from dipole-dipole and dipole-induced dipole attractions in polar molecules, and dispersion forces with non-polar substances.

5) Hydrophobic Bonds (Hydrophobic Effect):

These are also some of the weakest interactions. Indirect bonds (such groups only attract to each other) occur when non-polar groups are present in an aqueous solution. Water molecules adjacent to non-polar groups form hydrogen bonded structures that lower the system entropy. Thus, the tendency of non-polar groups to associate with each other increases to minimise this effect.

III. THEORIES OF BIOADHESION

The process of bioadhesive can be complex and involves more than one of the following theories:

1) Wetting Theory:

This theory is applied to liquid systems and takes into account surface and interfacial energies. It involves the ability of a liquid to spontaneously spread on a surface as a pre-requisite for adhesion development.

Spreading coefficient (SAB) can be calculated from the surface energies of the solid and liquids using the equation:

$SAB = \gamma B - \gamma A - \gamma AB$ ..... (1)

Where γA is the surface tension (energy) of the liquid A, γB is the surface energy of the solid B and γAB is the interfacial energy between the solid and liquid. SAB should be positive for the liquid to spread spontaneously over the solid. The work of adhesion (WA) represents the energy required to separate the two phases and is given by:

$WA = \gamma B - \gamma A - \gamma AB$ ..... (2)

Greater the individual surface energies of the solid and liquid relative to the interfacial energy, the greater the work of adhesion.

2) Electronic Theory:

As per this theory, electron transfer occurs across contacting adhering surfaces due to differences in their electronic structure. This results in the formation of an electrical double layer, which is adhered to the interface due to attractive forces.

3) Adsorption Theory:

This theory defines the attachment of adhesives due to hydrogen bonds and Van der Waal forces. These forces mainly contribute to the adhesive interaction. As per the chemisorption theory (a sub-section of adsorption theory), an interaction across the interface occurs due to strong covalent bonds.

4) Diffusion Theory:

This theory defines the inter-diffusion of polymer chains across an adhesive interface driven by concentration gradients. This is affected by the available molecular chain lengths, the compatibility of two polymers and their mobilities. The diffusion coefficient and the contact time influence the depth of inter-penetration. If the penetration depth is sufficient, a semi-permanent adhesive bond is formed.

5) Mechanical Theory:

As per this theory, adhesion arises from an interlocking of a liquid adhesive (on setting) into irregularities on a rough surface. Rough surfaces also provide an increased surface area for interaction along with an enhanced viscoelastic and plastic dissipation of energy during joint failure, which are important in the adhesion process.

6) Fracture Theory:

This theory relates the adhesive strength to the forces required for detaching the two involved surfaces after adhesion. This theory assumes that the failure of adhesive bond occurs at the interface. However, failure occurs at the weakest component, which is a cohesive failure within one of the adhering surfaces.

IV. MECHANISM OF MUCOADHESION

The mucoadhesion process due to relative complexity cannot be described by any one of these theories. The mechanism of mucoadhesion involves a whole range ‘scenarios’ for in-vivo mucoadhesive bond formation (figure 1) including:

1) Dry or partially hydrated dosage forms contacting surfaces with substantial mucus layers (particulates administered in the nasal cavity).

2) Fully hydrated dosage forms contacting surfaces with substantial mucus layers (particulates of many ‘first generation’ mucoadhesives become hydrated in the luminal contents on delivery to the lower GIT).

3) Dry or partially hydrated dosage forms contacting surfaces with thin/discontinuous mucus layers (tablets or patches administered in the oral cavity or vagina).

4) Fully hydrated dosage forms contacting surfaces with thin/discontinuous mucus layers (aqueous semisolids or liquids administered in the oesophagus or eye).

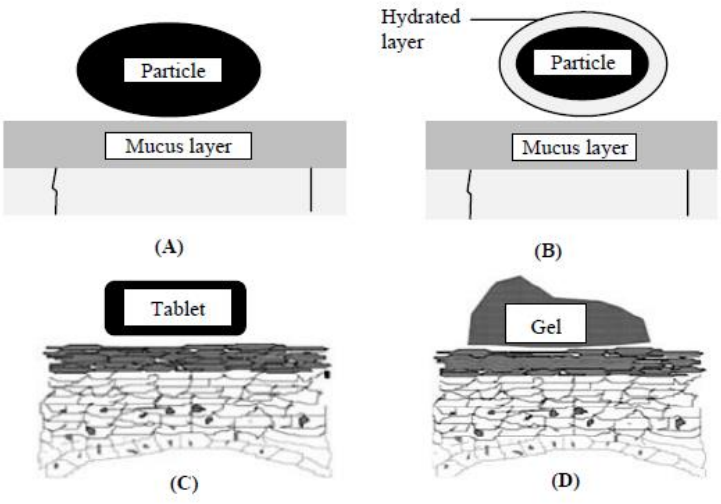

Figure 1: Mucoadhesion Occurrence in Different Scenarios

The adhesion mechanism of some macromolecules to the surface of a mucus tissue is still not clear. The mucoadhesive should spread over the substrate to maintain a close contact and increase the surface contact, thus promoting diffusion of its chains within the mucus. Attraction and repulsion forces arise, and the attraction forces should dominate to make the mucoadhesive successful. Each step is facilitated by the dosage form nature and its administration method.

The mechanism of mucoadhesion is divided into the following two stages:

1) Contact Stage:

The mucoadhesive and mucous membrane initially come together to form a close contact. Sometimes, these two surfaces are mechanically brought together by placing and holding a delivery system in the oral cavity, eye, or vagina. Some other times, a particle is deposited by aerodynamics of the organ; for example, particle deposition on the sticky mucus coat in the nasal cavity or bronchi of respiratory tract is facilitated by inertial impaction to filter out particles from the air stream.

2) Consolidation Stage:

For a strong or prolonged adhesion (such as with larger formulations exposed to stresses, such as blinking or mouth movements), a second consolidation stage is required. Mucoadhesive materials strongly adhere to solid dry surfaces till the time they are activated by the presence of moisture. Moisture effectively plasticise the system, thus making the mucoadhesive molecules free, allowing them to conform to the shape of the surface, and bind by weaker Van der Waal forces and hydrogen bonds.

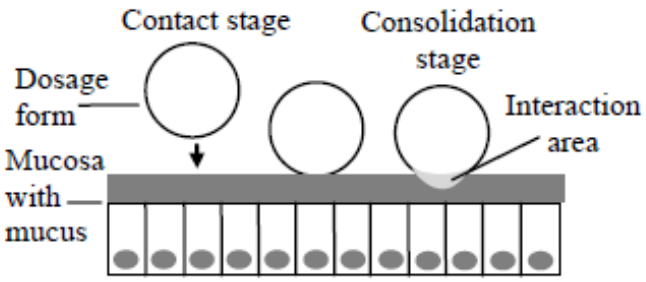

Figure 2: Two Stages in Mucoadhesion

The consolidation stage can be principally explained by two theories:

i) Diffusion Theory:

According to this theory, the mucoadhesive molecules and the mucus glycoproteins interact by inter-penetration of their chains and build-up of secondary bonds. This happens as the mucoadhesive device exhibits features that favour chemical and mechanical interactions. ii) Dehydration Theory: According to this theory, when the materials that can readily form into gels in an aqueous environment, are placed in contact with the mucus, they undergo dehydration due to the difference of osmotic pressure.

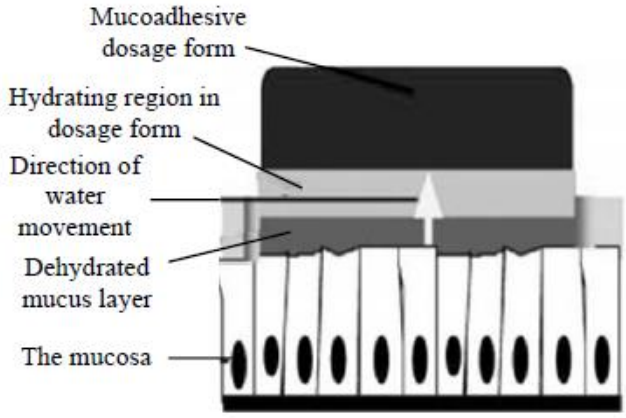

Figure 3: Dehydration Theory of Mucoadhesion

V. FACTORS AFFECTING MUCOSAL ADHESION

The given factors affect mucoadhesion as follows:

1) Polymer-Related Factors:

These include the following:

i) Molecular Weight:

Inter-penetration of polymer molecule is favourable for low molecular weight molecules, while entanglements are favoured for high molecular weight polymers. Optimum molecular weight for maximum bioadhesion depends on the polymer types. Their nature dictates the degree of swelling in water, which in turn determines inter-penetration of polymer molecules in the mucus. Bioadhesive forces increase with the molecular weight (up to 100,000 and not much effect is produced beyond this level). For chain inter-penetration, the polymer should be of adequate length, and its size and configuration are also important factors.

ii) Concentration of Active Polymer:

An optimum concentration of polymer is required for achieving the best bioadhesion. In highly concentrated system, the adhesive strength decreases; while in concentrated solutions, the coiled molecules become solvent poor andnot many chains are available for inter-penetration. These results are, however, for liquid bioadhesive forms. For solid dosage forms (such as tablets), higher the polymer concentration, stronger is the bioadhesion.

iii) Flexibility of Polymer Chains:

This factor is important for inter-penetration. The water-soluble polymers become cross-linked, and this reduces the mobility of individual polymer chain. With the increase in cross-linking density, the effective chain length that can penetrate the mucus layer decreases more, and mucoadhesive strength is thus reduced.

iv) Spatial Conformation:

This factor, along with molecular weight or chain length, is also significant. Despite a high molecular weight of 1,95,00,000, the adhesive strength of dextran is similar to that of PEG, having a molecular weight of 200,000. The helical conformation of dextran, unlike PEG polymers having a linear conformation, shields numerous adhesively active groups that are responsible for adhesion.

2) Environment-Related Factors:

These include the following:

i) pH:

It has a significant effect on mucoadhesion. pH influences the charge present on the surface of mucus as well as polymers. Mucus carries a different charge density depending on pH because of differences in dissociation of functional groups on the carbohydrate moiety and amino acids.

ii) Applied Strength:

A solid bioadhesive system can be maintained by applying a defined strength. The adhesion strength increases optimally with the applied strength or with the duration of its application, irrespective of the polymer. The pressure initially applied to the mucoadhesive tissue contact site affects the inter-penetration depth. If high pressure is applied for an extended time period, the polymers become mucoadhesive even though they are not attractively interacted with mucin.

iii) Initial Contact Time:

It is the time between mucoadhesive, and the mucus layer determines the extent of swelling and the inter-penetration of polymer chains. The initial contact time, along with the initial pressure, can affect the system performance. Mucoadhesive strength increases with the increase in initial contact time. Initial contact time is critical in case of mucoadhesive that need to be polymerised at the application site.

iv) Swelling:

This factor is related to the polymer, and its environment. Since the polymer chains are disentangled and free of interactions, their inter-penetration is easier. Swelling depends on polymer concentration and presence of water. When swelling is more, bioadhesion decreases. This phenomenon should not occur too early to result in a sufficient action of bioadhesive system. Its appearance allows easy detachment of bioadhesive system after the discharge of active ingredient.

3) Physiological Variables:

These include the following:

i) Mucin Turnover:

The natural turnover of mucin molecule from the mucus layer is important for two reasons:

a) Mucin turnover limits the residence time of the mucoadhesives on the mucus layer, thus detaching the mucoadhesives from the surface.

b) Mucin turnover results in extensive amounts of soluble molecules that interact with mucoadhesives before they interact with the mucus layer. This type of surface fouling does not favour mucoadhesion to the tissue surface.

ii) Diseased State:

Physicochemical properties of mucus alter during diseased conditions, such as common cold, gastric ulcers, ulcerative colitis, cystic fibrosis, bacterial and fungal infections of the female reproductive tract, and inflammatory conditions of eye. If mucoadhesives are to be used in the diseased states, its mucoadhesive property should be evaluated under the same condition.

VI. TRANSMUCOSAL PERMEABILITY

Two routes are involved in drug permeation across epithelial membranes, i.e., the transcellular route and the paracellular route. In the studies of mechanisms of trans-membrane permeation, the epithelial membrane structure is simplified to consist of a lipoidal pathway and an aqueous pore pathway (figure 4.4). Skin and gastrointestinal mucosa are considered lipoidal barriers, in which the drug absorption is determined by the magnitude of its partition coefficient and molecular size, till the diffusion through aqueous diffusion layer (Pa) becomes a rate-limiting step in trans-membrane permeation. Several researchers have observed lack of a linear correlation between penetrant lipophilicity (indicated by the partition coefficient magnitude) and permeability. This implies that these membranes are not simple lipoidal barriers.

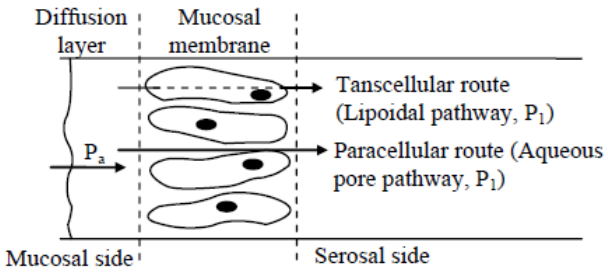

Figure 4: Physical Model for Trans-Membrane Permeation across a Mucosal Membrane consisting of Lipoidal and Aqueous Pore Pathways in Parallel, which is in series with an aqueous diffusion layer on the mucosal surface. P's are the permeabilities across the aqueous diffusion layer (Pa), the lipoidal pathway (Pb), and the aqueous pore pathway (Pb)

For nasal mucosal membrane an experiment was performed to prove the existence of a lipoidal and an aqueous pore pathway. The rate and extent of nasal absorption of β-adrenoreceptor-blocking drugs in humans were related to the lipophilicity of drugs (the most lipophilic propranolol achieved the highest absorption). The rate constant for in situ absorption of progesterone, testosterone, and hydrocortisone in rats and the lipophilicity of steroids were found to be proportional. However, several studies indicate that a permeant's absorption is affected by its lipophilicity, still it does not alone determines the rate and extent of nasal absorption.

It has been suggested that the nasal mucosa serves as a modified lipoidal barrier for lipophilic permeants. The pH-partition theory (absorption depends on the concentration of undissociated species of a permeant molecule) is not applicable for many hydrophilic drugs. It has also been reported that the logarithm of nasal absorption and the logarithm of drug molecular weights are linearly correlated for many water-soluble compounds. This indicates the presence of aqueous pore channels in the nasal mucosa for the absorption of hydrophilic drugs.

Transmucosal permeation of polar molecules (such as peptide-based pharmaceuticals) occurs through paracellular route; however, the following barriers exist during the paracellular permeation:

1) The barrier function of basal lamina depends on the molecular weight of the permeant molecule, its reactivity with the barrier, and the structural and functional factors of the barrier.

2) Membrane-coating granules extrude into the intercellular region of keratinised and non-keratinised oral epithelium and prevent the transmucosal penetration of water-soluble peptide or protein, such as horseradish peroxidase.

3) The barrier function of keratin layer in oral mucosa is not as well-defined as in the skin. The permeation rate of water was shown to be greater in non-keratinised than in keratinised oral epithelium, but the permeation of horseradish peroxidase was found to be similar in both mucosae.

4) The permeability coefficients of 19 solutes across the rabbit lingual frenulum and attached gingiva were determined under in vitro conditions. They were found correlated, suggesting that the epithelia from different regions of the oral mucosa are similar in mechanisms and rates of trans-mucosal permeation.

In comparison to the complexity of nasal and oral mucosae, drug absorption through rectal mucosa follows the pH-partition theory. It has been established that ionic and lipid-insoluble drugs are poorly absorbed and the lipid-soluble drugs are rapidly absorbed on rectal administration. It was reported that the rectal mucosa of rats have a poorer distribution of aqueous pore channels than other regions of the GIT, including the jejunum. The correlation between rectal absorption of drugs and their partition coefficients implies that rectal mucosa can be considered as a simple lipoidal barrier.

The vaginal mucosal membrane, similar to the nasal mucosa, comprises of a lipoidal pathway and an aqueous pore pathway. In the vaginal mucosa of rabbits, the permeability coefficient of aliphatic alcohols increases with the increase in their lipophilicity; thus, indicating the importance of lipoidal pathway in vaginal permeation. The aqueous diffusion layer on the rabbits' vaginal mucosal surface was estimated to be approximately 310nm thick.

VII. FORMULATION CONSIDERATIONS OF BUCCAL DELIVERY SYSTEMS

Following are the basic formulation requirements of buccal drug delivery system:

1) Drug:

Before mucoadhesive drug delivery systems are formulated, it should be decided that whether the intended action is for rapid release, prolonged release, local effect, and/or systemic effect. A suitable drug should be selected based on its pharmacokinetic properties for designing buccoadhesive drug delivery systems.

The drug should have the following characteristics:

i) The conventional single dose of the drug should be small.

ii) The drugs with biological half-life of 2-8 hours are good candidates for controlled drug delivery.

iii) The drug tmax shows wider-fluctuations or higher values on oral administration.

iv) The drug may undergo first pass effect or pre-systemic drug elimination on oral administration.

v) The drug undergoes passive absorption on oral administration.

2) Bioadhesive Polymers:

Selection and characterisation of appropriate bioadhesive polymers is the first step in the development of buccoadhesive dosage forms. These polymers are important in buccoadhesive system of drug delivery. Polymers are also used in matrix devices, in which the drug is embedded in the polymer matrix, which control the duration of drug release. Bioadhesive polymers are from the most diverse class and substantially benefit the patient health care and treatment. The drug is released in the mucous membrane via rate controlling layer or core layer. Bioadhesive polymers adhered to the mucin/epithelial surface are effective and significantly improve the oral drug delivery.

The ideal characteristics for a polymer and its degradation products for buccoadhesive drug delivery systems are:

i) It should be inert and compatible with the environment.

ii) It should be non-toxic and absorbable from the mucus layer.

iii) It should allow easy incorporation of drug in the formulation.

iv) It should quickly adhere to moist tissue surface and should possess site specificity.

v) It should not decompose on storage or during the shelf-life of the dosage form.

vi) It should be economical and easily available in the market. Examples of some commonly used mucoadhesive polymers in pharmaceutical applications are enlisted in table

Table 1: Mucoadhesive Polymers used in the Oral Cavity

S. No	Polymers	Mucoadhesive Property
1.	Carbopol 934	+++
2.	Carboxymethylcellulose	+++
3.	Polycarbophil	+++
4.	Tragacanth	+++
5.	Sodium alginate	+++
6.	Hydroxymethylcellulose	+++
7.	Gum karya	+++
8.	Guar gum	++
9.	Polyvinylpyrrolidone	++
10.	Polyethylene glycol	+
11.	Hydroxypropyl cellulose	+

3) Backing Membrane:

It plays an important role in the attachment of bioadhesive devices to the mucus membrane. Inert materials should be used as a backing membrane. These materials should also be impermeable to the drug and penetration enhancer. The resultant impermeable membrane on buccal bioadhesive patches prevents drug loss and improves patient compliance. Carbopol, magnesium stearate, HPMC, HPC, CMC, polycarbophil, etc. are the examples of some commonly used backing membrane material.

4) Plasticisers:

These are used for achieving softness and flexibility of thin films of polymers. They also act as permeation enhancers. Glycerol, PEG200, PEG400, castor oil, etc. are the examples of some commonly used plasticisers. A suitable plasticiser is selected depending on the ability of plasticiser material to solvate the polymer and alters the polymer-polymer interactions. If the plasticiser is used in correct proportion to the polymer, it relieves molecular rigidity and imparts flexibility.

5) Permeation Enhancers:

These substances facilitate permeation through buccal mucosa. A suitable permeation enhancer is selected based on the physicochemical properties of the drug, administration site, nature of the vehicle and other excipients.

The mode of action of penetration enhancers is as follows:

i) They alter the mucus rheology by reducing the viscosity of the mucus and saliva overcomes this barrier.

ii) They increase the fluidity of lipid bilayer membrane, disturb the intracellular lipid packing by interacting with either lipid or protein components.

iii) They act on the components at tight junctions by inhibiting various peptidases and proteases present in the buccal mucosa, thus overcoming the enzymatic barrier. They also change membrane fluidity, which in turn alters the enzymatic activity.

iv) They increase the thermodynamic activity of drugs by increasing their solubility, thereby altering their partition coefficient.

Table 2 enlists the common examples of permeation enhancers, along with their mechanisms:

Table 2: Examples of Permeation Enhancers with their Mechanism

Categories	Examples	Mechanism(s)
Surfactants and Bile Salts	Surfactants and bile salts, sodium dodecyl sulphate, sodium lauryl sulphate, and polysorbate 80.	Act on the components at tight junctions; increase the fluidity of lipid bilayer membrane.
Fatty Acids	Oleic acid, cod liver oil, capric acid, and lauric acid.	Increase the fluidity of lipid bilayer membrane.
Polymers and their Derivatives	Chitosan, trimethyl chitosan, and chitosan–4–thiobutylamide.	Increase the fluidity of lipid bilayer membrane; Increase the retention of drug at mucosal surface.
Others	Ehanol, azone, octisalate, padimate, and menthol.	Act on the components at tight junctions; Increase the fluidity of lipid bilayer membrane

6) Preservatives:

Parabens, benzalkonium chloride, phenyl ethyl alcohol, EDTA, and benzoyl alcohol are the examples of some commonly used preservatives.

Manufacturing Methods of Buccal Patches:

The manufacturing processes for mucoadhesive buccal patches/films are discussed below:

1) Solvent Casting: In this method, the drug and the patch excipients are dispersed in an organic solvent and coated on a sheet of release liner. After the solvent evaporates, a thin layer of protective backing material is laminated on the sheet of coated release liner. This forms a laminate that is die-cut to form patches of desired size and geometry.

2) **Direct Milling:** In this method, patches are manufactured without using solvents. The drug and excipients are mechanically mixed by direct milling or by kneading in the absence of any liquid. After mixing, the obtained material is rolled on a release liner to obtain the desired thickness. Then the backing material is laminated as in the solvent casting me thod. There are minor or no differences at all in the patch performance between the patches fabricated by solvent casting and direct milling, thus the solvent-free process is preferred as residual solvents are not formed and solvent -related health issues do not occur.

3) **Hot Melt Extrusion of Films:** In this method, a blend of pharmaceutical ingredients is molten and forced through an orifice to obtain a homogeneous material in the form of granules, tablets, or films. The method of hot melt extrusion has been u sed for manufacturing controlled release matrix tablets, pellets, granules, and oral disintegrating films.

VIII. EVALUATION

In vitro/ex vivo tests:

- Tensile strength
- Shear stress
- Fluorescent probe method
- Falling liquid film method
- Colloidal gold staining method
- Viscometer method
- Thumb method
- Adhesion number
- Swelling properties
- Stability studies

In vivo methods:

- Use of radio opaque markers
- Use of gamma scintigraphy
- X ray studies
- Isolated loop technique
- Use of electron paramagnetic resonance

Different Dosage Form of MDDS:

The dosage form of oral drug delivery system are as follows:

- Buccal tablets
- Bioadhesive film\patches
- Buccal liposomes
- Buccal gels and ointments
- Bioadhesive lozenges
- Medicated Chewing gum

Example-Buccastem, Susgard, Corsodyl Gel

Ophthalmic/occular dosage form are as follows:

- Ocular nanoparticles
- Ocular liposomes
- Ocular microspheres
- Ocular inserts

Example- Nyogel, Hyotears, PiloGel

Nasal dosage form are as follows:

- Nasal microspheres
- Nasal liposomes

Example- Rhincort, Nasacart

Gastrointestinal dosage form are as follows:

- Gastric floating tablets
- Gastric floating capsules
- Floating pills

- Swellable tablets

Example- Coreg CR, Liquid Gaviscon, Nucarnit M

Vaginal dosage form are as follows:

- Pessaries
- Vaginal topical administration
- Vaginal tablets
- Vaginal microspheres

Example- Crinone, Acid Gel

IX. CONCLUSION:

Mucoadhesive drug delivery systems are becoming increasingly popular. Extensive research worldwide has led to significant advancements in understanding various aspects of mucoadhesion. There is no doubt that mucoadhesion has entered a new era with the development of specific targeting compounds such as lectins and thiomers. These dosage forms provide prolonged contact at the administration site, low enzymatic activity, and improved patient compliance. Formulating mucoadhesive drug delivery systems relies on selecting polymers with excellent mucoadhesive properties and biocompatibility. This review focuses on studying different aspects of mucoadhesion, including the structure of the mucus membrane, mucoadhesive theories, and formulation techniques. While significant progress has been made in this field, challenges remain. Nevertheless, novel mucoadhesive formulations have been developed for treating both systemic and topical diseases.

X. REFERENCE:

[1] Anjana Anil, et al., Mucoadhesive Polymer: A Review, Journal of Pharmaceutical Research, Volume 17, Issue 1, Jan-Mar, 2018 Page No.48-50

[2] B Phanindra, et al., Recents Advances in Bioadhesive\Mucoadhesive Drug Delivery System: A Review, Int. J. Pharm. Med. & Bio. Sc. Vol. 2, No. 1, January 2013, Page no.69-73 1

[3] Carvalho Flávia Chiva, et al., Mucoadhesive drug delivery systems, Brazilian Journal of Pharmaceutical Sciences vol. 46, n. 1, jan./mar., 2010 Page no.2

[4] Dhiman Sonia, Dhiman Hardik, et al., Mucoadhesion Drug Delivery Sytem: A Propitious Approach, International Journal Pharm. Sci. Rev. Res., 50(2), May -June 2018; Article No. 12 Page no. 72

[5] Kaur Saini Harvinder, et al., A Review Article on Pioneering and Encouraging Approach, Mucoadhesive Drug Delivery System, Int. J. Pharm. Med. Res. 2017; 5(3):455-463Page no.455

[6] Khan Shahid, et al., Mucoadhesive Drug Delivery System: A Review, World Journal of Pharmacy and Pharmaceutical Sciences, Vol 5, Issue 5, 2016 Page no.392-395

[7] Kharenko E.A.et al., A Review on Mucoadhesive Drug Delivery System, Pharmaceutical Chemistry Journal, Vol. 43, No. 4, 2009 Page no. 200

[8] Kumari Navita, et al., Mucoadhesive Microspheres: A Review, Journal of Drug Delivery & Therapeutics; 2014, 4(5), Page no.49-50

[9] Lokhande Sachin Shankar, et al., Buccoadhesive Drug Delivery System, Asian Journal of Biomedical and Pharmaceutical Sciences, Volume2, Issue 14, 2012, Page no.30-32

[10] Madan Jyotsana, et al., Mucoadhesive Drug Delivery System, International Journal of Research in Ayurveda & Pharmacy, Volume 1, Issue 1, Sep-Oct 2010 page no.63-70

[11] Muthukumaran M,et al., A Review on Polymer used Mucoadhesive Drug Delivery System, Int. J. Pharm & Ind. Res Vol-01 issue-02Apr-Jun2011,Page no. 123

[12] N Miller, etal, The Use of Mucoadhesive Polymers in Buccal Drug Delivery, Advanced Drug Delivery Reviews,2005;57:1669- 1691

[12] Pandey Parijat, et al., Mucoadhesive drug delivery system: an overview Pharmaceutical and Biological Evaluations2017; Vol. (4), Page no.183-185

[13] Parmar Hitanshi Kulinsinh, et al., A Systemic Review on mucoadhesive drug delivery system, World Journal of Pharmaceutical Research, Vol 6, Issue 09, 2017, Page no.337

[14] Singh R, et al., Review on Mucoadhesive Drug Delivery System with Special Emphasis on Buccal Route: An Important Tool in Designing of Novel Controlled Drug Delivery System for the Effective Delivery of Pharmaceuticals J Dev Drugs, Volume 6 Page no.1-5

[15] Yadav Vimal Kumar et al., Mucoadhesive Polymers: Means of Improving the Mucoadhesive Properties of Drug Delivery System, Journal of Chemical and Pharmaceutical Research, Page no.418-421