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A Review On Mucoadhesive Drug Delivery System

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Abstract

Drug delivery methods that are mucoadhesive prolong the dosage form's period of residence at the application or absorption site. They enable a close contact between the dose form and the underlying absorption floor, which improves the drug's total capacity for healing. These structures are still in close contact with the mucosal membrane, the absorption tissue, and the site of action, which leads to a rise in bioavailability and both local and systemic effects. The main advantage of using this route for medication delivery is that it bypasses the hepatic first pass metabolism of many capsules, which is vulnerable to this route's effects. By briefly discussing the structural function of the mucosa, the mechanism of mucoadhesion, various theories of mucoadhesion, well-known attention in the design of mucoadhesive buccal dosage forms, permeation complements, and various assessment strategies along with the literature survey of the mucoadhesive drug transport System, this assessment provides the brief information about the oral mucosal drug transport.

Keywords

Mucoadhesive, mucous, Mucoadhesion, polymer, bioavailability, transport

Introduction

The concept of mucoadhesion has advanced pharmaceutical technology significantly since the early 1980s.[1] The link created by contact between a floor and a stress-sensitive adhesive is known as adhesion. It is the nation where surfaces are held together by interfacial forces, which can also include valence forces, interlocking motion, or both, according to the American Society of Testing and Materials. Drug delivery systems that adhere to the mucosa extend the residence period of the dose form on the page of software or absorption. Recent years have seen the development of numerous mucoadhesive drug transport structures for oral, buccal, nasal, rectal, and vaginal routes for both systemic and local effects [2]. It is possible to concentrate a medicine to a specific area of the body for extended periods of time by using mucoadhesive drug transport structures, which leverage the advantages of bioadhesion of positive polymers that become adhesive during hydration. Two materials, at least one of which is unquestionably acknowledged to be organic, are held together by interfacial forces in a process known as bioadhesion. The attachment may involve adhesion between a polymer and an organic membrane as well as between a synthetic fabric and an organic substrate. The word "mucoadhesion" refers to the connection of a polymer to the mucin layer of a mucosal tissue [3].

The mucus membrane (additionally known as mucosa) is a wet tissue lining that covers the organs and cavities which includes the mouth, nose, eyelid, gut, and rectum. Leung and Robinson describe mucoadhesion because the interplay among a mucous floor and a artificial or herbal polymer. The polymer service containing healing fabric will adhere to the focused mucosa for an prolonged period, thereby growing its permeation and bioavailability. Many readers may also confuse the term “mucoadhesion” with “bioadhesion”. 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) sublingual transport, systemic transport of healing compounds via the mucosal floor of the mouth;

(ii) buccal transport, management via the mucosal linings of cheeks (buccal mucosa)

(iii) neighborhood transport, management via the oral cavity.

Rout Of Mucoadhesive Drug Delivery System.

Sublingual delivery is advantageous for the rapid commencement of healing motion (for example, sublingual nitroglycerin for the treatment of Angina pectoris) and the buccal mucosa is generally relevant for medication management [4]. The mucoadhesion theory has generated a lot of interest in the pharmaceutical industry and is successfully applied as a management strategy. Mucoadhesive drug transport structures may be brought via way of diverse routes:-

• Buccal delivery system

• Oral delivery system

• Vaginal delivery system

• Rectal delivery system

• Nasal delivery system

• Ocular delivery system [5]

1.Buccal Delivery System

One alternative to oral drug management, particularly for capsules that have a first-by-skip effect, is buccal administration of medication. The buccal mucosa's stratified squamous epithelium, which is maintained by the connective tissue lamina propria, was previously targeted as a website for drug delivery. The buccal approach appears to have various advantages, including precise accessibility, epithelial toughness, use of the dosage form in accordance with requirement, and generally considerably less susceptible to enzymatic activity. As a result, adhesive mucosal dosage paperwork was prepared for oral delivery and contained adhesive patches, gels, and tablets. The permeation of hydrophilic drug via membrane is one of the essential proscribing elements for theimprovement of bioadhesive buccal shipping devices.[6]

2.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. The most well-known and patient-friendly method of drug delivery is oral administration, even though this method has more serious risks due to the involvement of the gastro-intestinal (GI) system and drug bioavailability. Lipid-based entirely oral shipping structures researched updated emphasises the importance of each device component to the shipping performance and the oral shipping course of lipids.[7]

3.Vaginal Delivery System

Drug administration through vaginal birth is crucial for treating both systemic and local illnesses.An important component of medication treatment for both localised disorders and systemic diseases is vaginal delivery. Due to its large floor surface, abundant blood supply, avoidance of the first-by skip effect, particularly increased permeability to many capsules, and self-insertion, the vaginal route has a few advantages. The self-cleansing motion of the vaginal tract is thought to make it difficult for the traditional business preparations, such as creams, foams, gels, irrigations, and tablets, to remain inside the vaginal hollow space for very long periods of time. Therefore, it frequently takes several daily doses to achieve the desired healing effect [8].

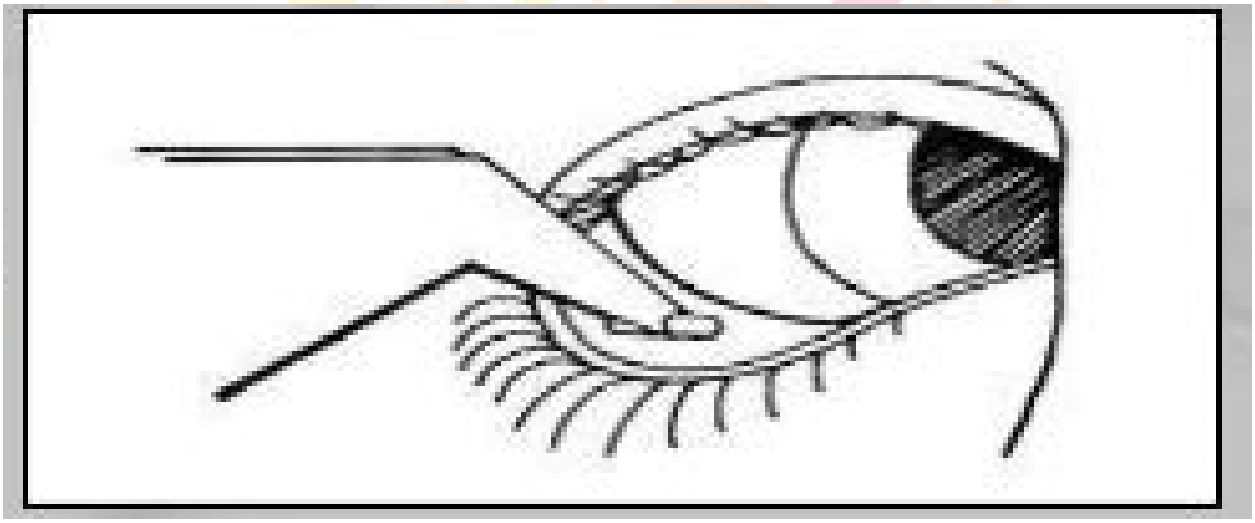
4.Rectal Delivery System

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. Mucoadhesion, or the drug's attachment to the mucous membrane in conjunction with a potent carrier, is provided by these structures.[9]

5. Nasal Delivery System

Nasal administration, also referred to as snorting, is a method of medication delivery in which the medicine is inhaled by the nose. In the drug absorption process, the floor, the drug awareness and quantity, the physical location of the dosage form, and the placement of the top at some point of management all play a role. 1) Locally sourced nasal drug shipping tablets 2) Shipping of systemic drugs 3) medication delivery from the nose to the brain 4. Nasal vaccination. [10]

6.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 cull-de sac of the eye. [11] Ophthalmic techniques or instructions are specialist sterile dosage instructions. The drug may be applied topically directly to the skin, intraocularly, or next to the eyes, periocularly, to the attention. By using the recommended medications and researchers, one of the most intriguing and difficult challenges of ODDS is met. [12]Ocular tablets are normally introduced domestically to the attention. Required drug loading, launch charge, and ocular retention time of drug shipping structures depend upon the potency, bioavailability, and clearance of the drug on the goal web page. [13]

Mucous Membrane

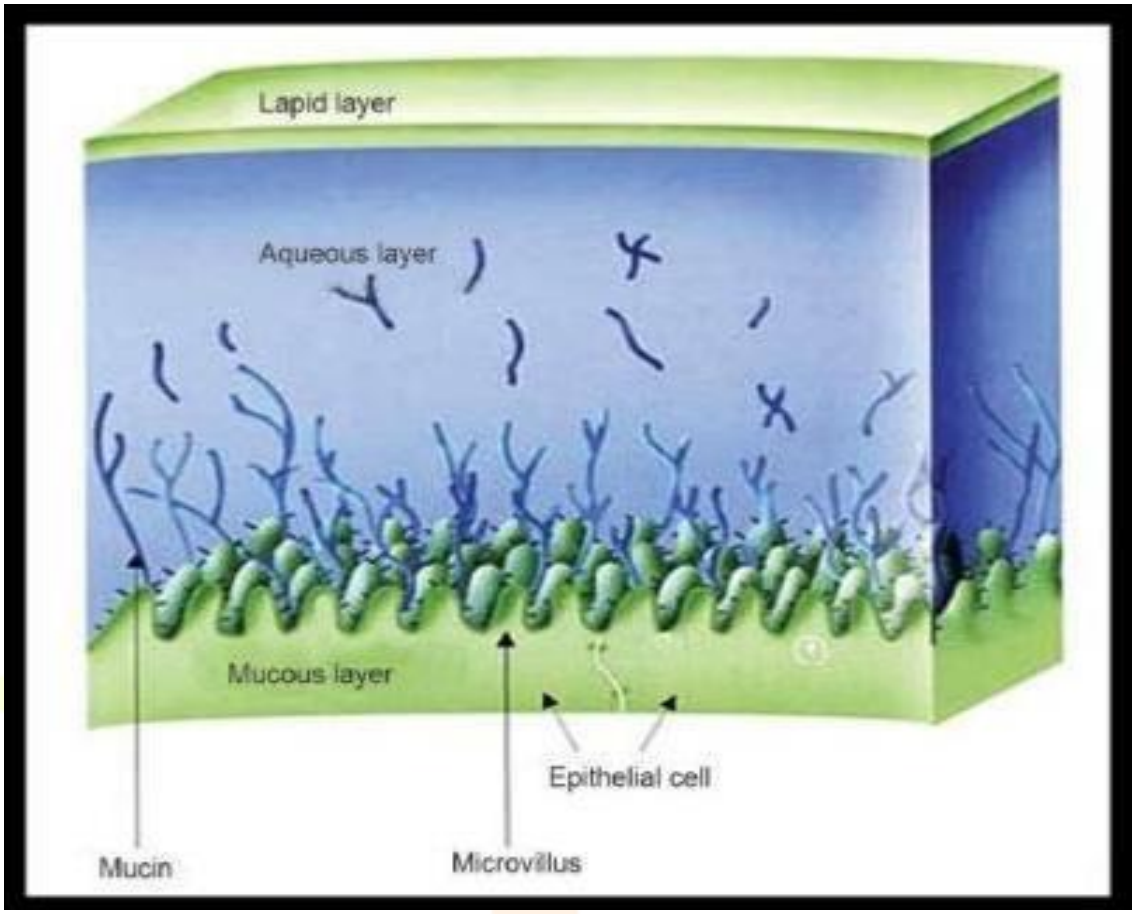


Figure 1:Mucous membrane structure

The wet surfaces that line the walls of several body cavities, including the gastrointestinal and respiratory systems, are known as mucous membranes (mucosae). The lamina propria, a connective tissue layer, sits on top of an epithelial layer, the floor of which is typically rendered wet by the presence of a mucus layer. The bronchi, small and large intestines, and the stomach are examples of single-layered epithelia. Other examples of multi-layered or stratified epithelia are the oesophagus, vagina, and cornea. Goblet cells, which release mucus immediately onto epithelial surfaces, are a component of the former; salivary glands and specialised glands, which secrete mucus onto the epithelial floor, are a component of the latter. Mucus is gift both as a gel layer Adherent to the mucosal floor or as a luminal soluble or Suspended form. Mucin glycoproteins, lipids, inorganic salts, and water are the main components in all mucus gels; the latter makes up more than 95% of their weight, making them a very hydrated machine. Mucus primarily functions as a lubricant and a safety net.[14]

Composition of mucus layer

The mucus is a fairly hydrophilic machine since it contains glycoproteins, lipids, salts, and 95% of its bulk is water. [15,16] Excessively high molecular weight proteins known as mucus glycoproteins have linked oligosaccharide

devices that contain L-fructose, D-galactose, N-acetyl-D-glucosamine, N-acetyl-D-galactosamine, and sialic acid. [17,18].

Functions of Mucus Layer:

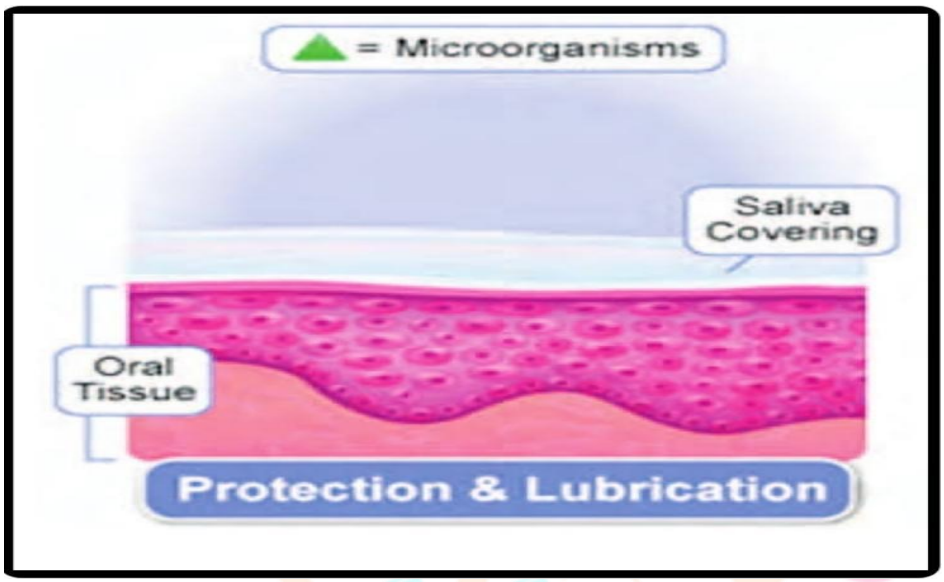


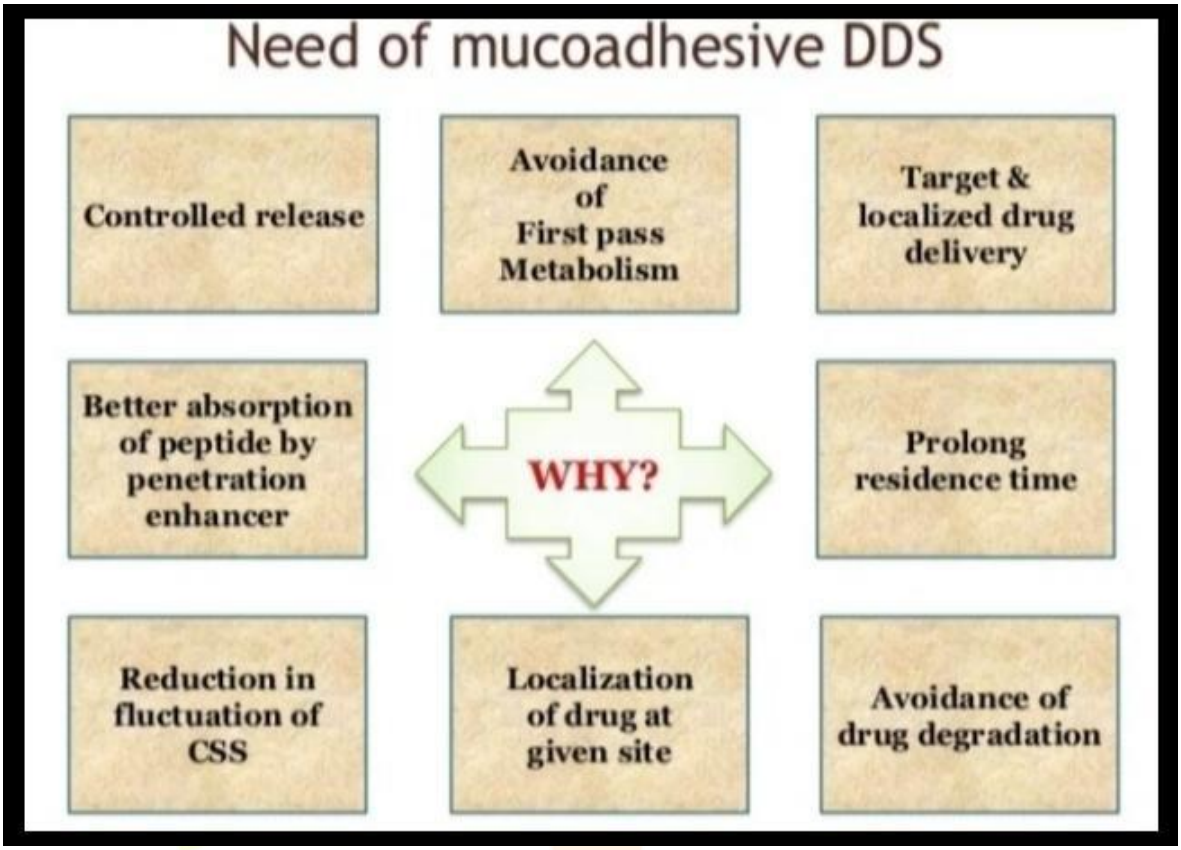
Figure 2.Function of Mucosa

1. **Protective**: ensuing in particular from its Hydrophobicity.
2. **Barrier**: The function of the mucus layer as a barrier In tissue absorption of the medication and impact The bioavailability.

3. Adhesion: Mucus has robust adhesion Properties.

4. Lubrication: It is to preserve the mucus from the Goblet molecular is vital to make amends for the Removal of the mucus layer because of digestion, Bacterial degradation and solubilisation of Mucin molecules.

Need of mucoadhesive drug delivery system



Flow Chart 1: Need of MDDS

Mechanism of mucoadhesion

Mucoadhesion is the process by which two materials—one that can be artificial with a mucoadhesive polymer and another that can be a mucin layer of the mucosal tissue—hold one other together by applying interfacial pressure.Mucoadhesive is a term used to describe a synthetic substance that interacts with mucus membranes and can be kept on them or keep them together for a lengthy period of time. During the technique of adhesion there have degrees recognized are given below.

1. Contact Stage

2. Consolidation degree

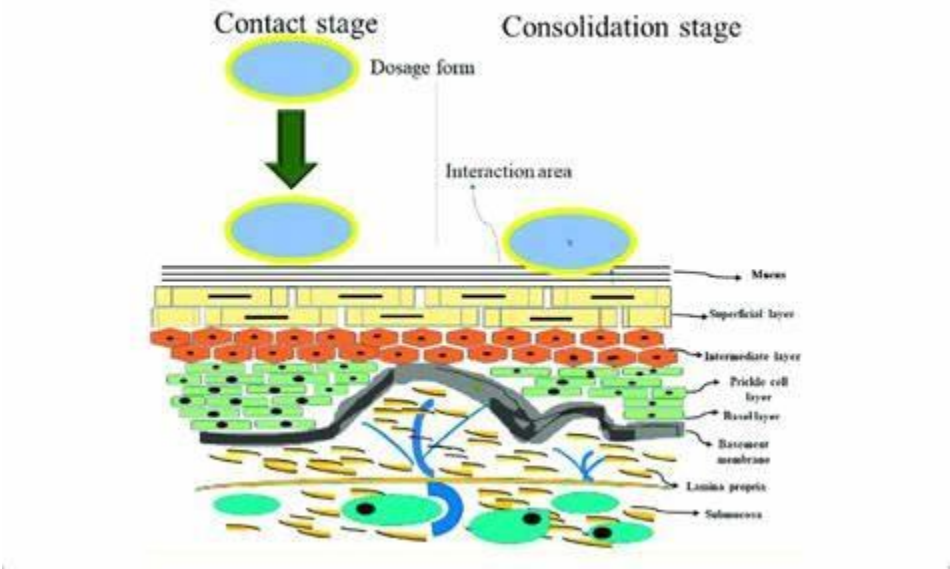


Figure No 3: Mechanism of mucoadhesion

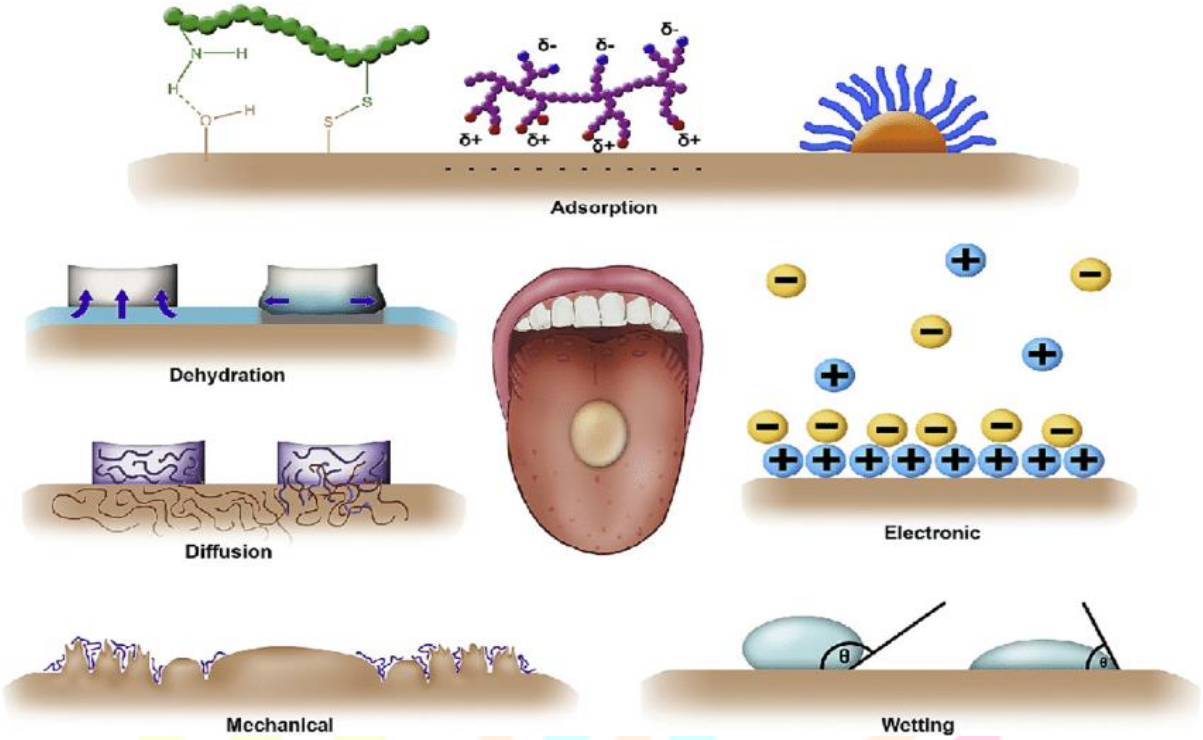
1.Contact Stage

At this point, when the mucoadhesive fabric makes contact with the mucous membrane, there is an intimate wetting between the mucoadhesive and the mucous membrane. This wetting of mucoadhesive is carried out through the mucus found in mucosal membrane.

2.Consolidation Stage

By utilising a combination of hydrogen bonding, van der Waals forces, and electrostatic and electrochemical enchantment forces. The mucus membrane is affected by the pressures present in mucoadhesive fabric, resulting in long-lasting adherence. Consolidation degree is the name given to this degree. The mucoadhesion procedure is finished at those degrees.[19]

Theories of Mucoadhesion



Flow Chart 2: Theories of mucoadhesion

1)The Electronic Theory:

According to this theory, changes in digital structure cause an electron switch to occur when a sticky polymer and the mucus glycoprotein community come in contact. It is thought that doing this will cause a digital double layer to form on the interface, followed by adhesion from attractive forces within the double layer.

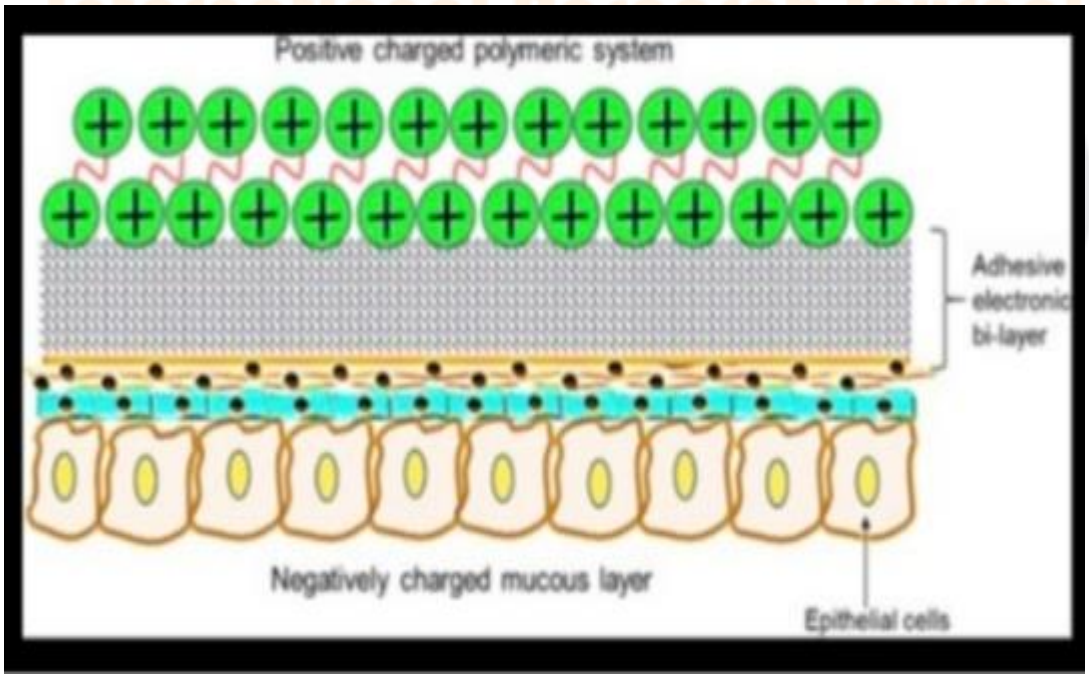


Figure No 4. Electronic concept of mucoadhesion

2)The wetting Theory:

It mostly applies to liquid frameworks and issues involving interfacial and floor energies. It includes the capacity for a fluid to spread instantly over a surface as a necessary component for the formation of a bond. When using techniques like touch attitude geometry to measure the liquid's touch attitude on the floor, the affinity of the liquid for the surface may be seen.

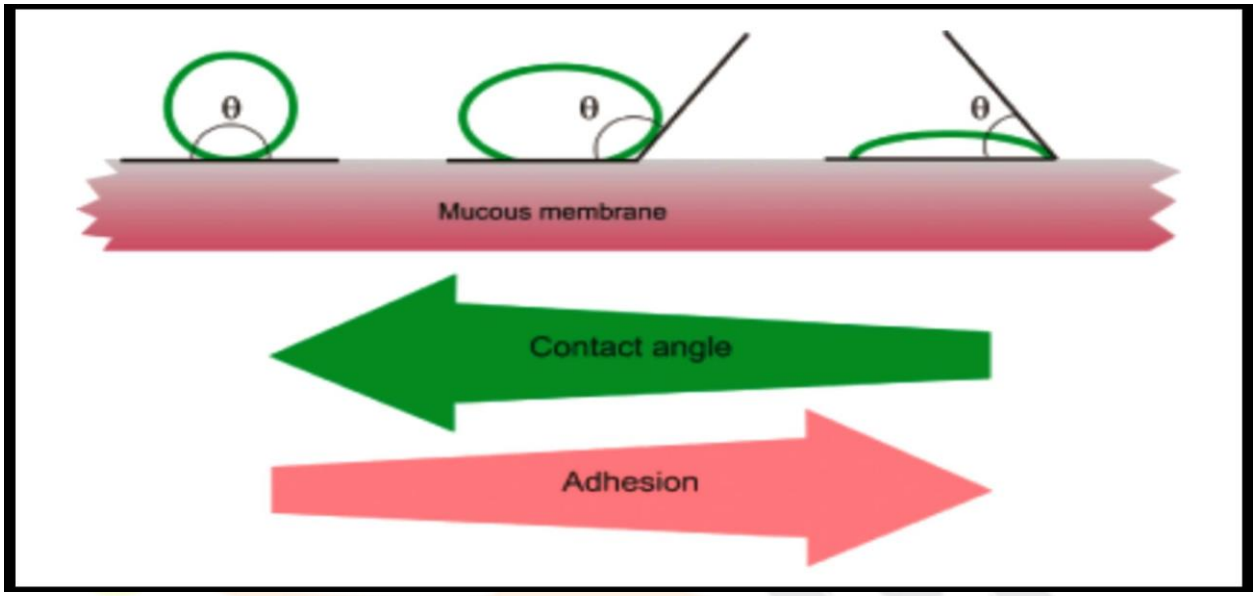


Figure No 5: Wetting concept of mucoadhesion

3)Adsorption Theory:

This theory bases sticky adhesion on the principles of hydrogen bonding and Vander Waals forces. There are two different types of chemical bonds: primary covalent and secondary chemical bonds, which include hydrophobic, Vander Waals, and electrostatic interactions.

4)The diffusion Theory:

According to this theory, the mucus and polymer chains combine well enough to form a link that is somewhat permanent. This approach is hampered by available molecular chain lengths and their mobility and is driven by a concentration gradient. It is dependent on the molecular weight of the cross links and falls noticeably when the go linking density goes down.

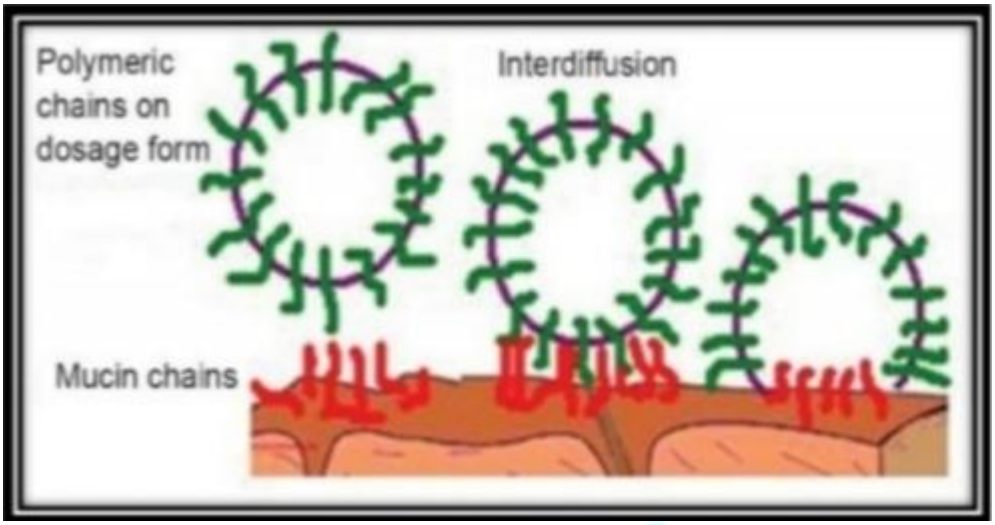


Figure No 6: Theory of Diffusion concept

5)The mechanical Theory:

This idea acknowledges the attachment emergency caused by fluid cement interlocking into anomalies on an unsightly floor. However, a hard surface also provides space on the growing floor for interaction with a more suitable viscoelastic and plastic dissipation of strength during joint failure, which is thought to be more important for adhesion than a mechanical effect.

6)The fracture Theory:

According to this concept of adhesion is associated with separation of floor after adhesion. The fracture power is same to adhesive power, it's far Given via way of means of,

G=(□□/L) ½… (equation 1)

E= Young's module of elasticity

□= Fracture strength elasticity

L = Critical crack period while surfaces are separated.[20]

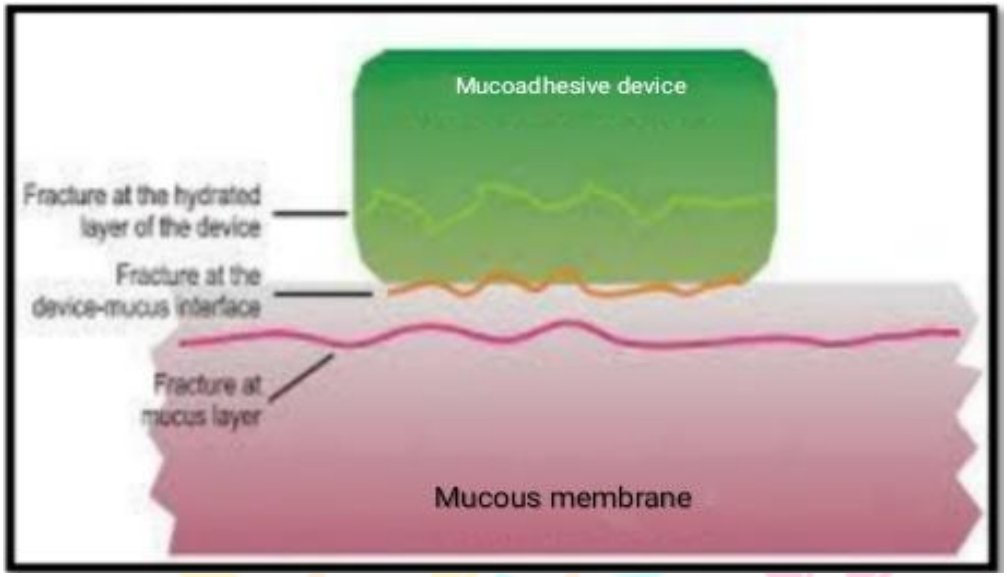


Figure No 7:Fracture principle of mucoadhesion

Mucoadhesive Polymers

Ideal Characteristics of Mucoadhesive Polymers:

The delivery of a mucoadhesion-promoting agent or polymer to the device enables the promotion of the adherence of the active medicinal ingredient to the oral mucosa. The chemical may possess additional properties including swelling with the intention of promoting breakdown even when in contact with saliva.

1) Long chain polymers-chain period must be prolonged Enough to promote the interpenetration and it want to now not be too prolonged that diffusion becomes a problem.

2) Degree of by skip linking- it influences chain mobility and resistance to dissolution. Highly by skip associated polymers swell in presence of water and keep their form.

3)Concentration of the polymer- an maximum beneficial interest is wanted to promote the mucoadhesive power. It is predicated upon but, on the dosage form.

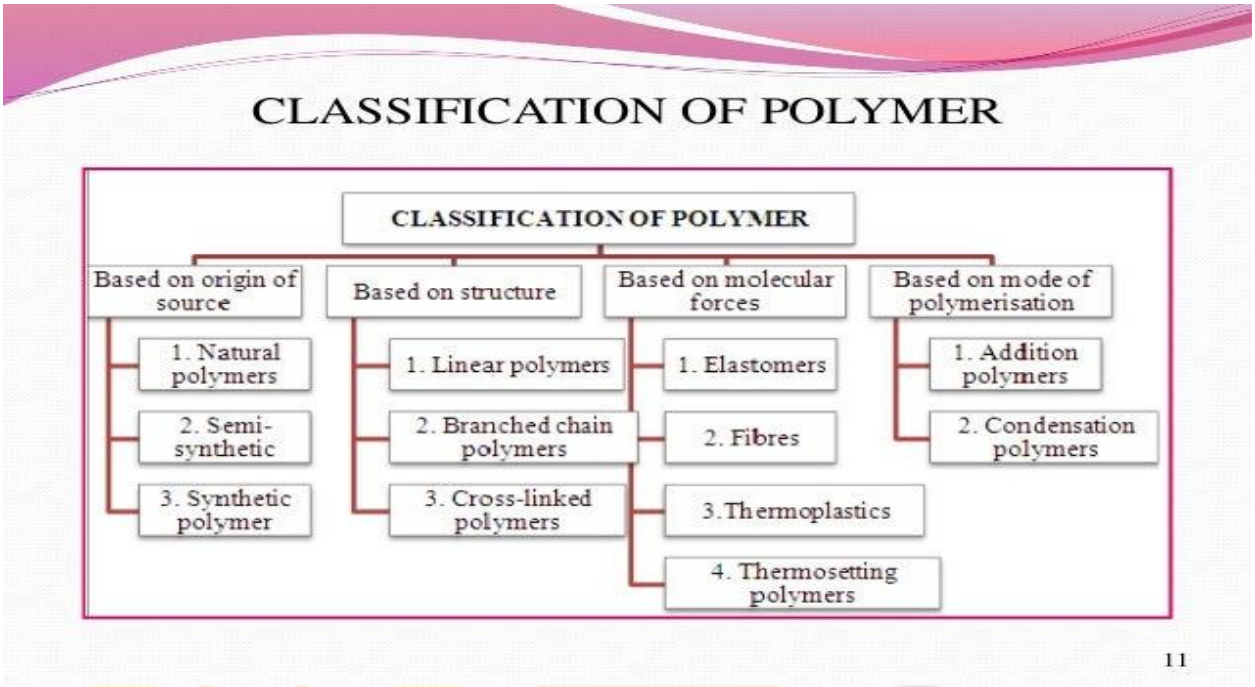
4) Charge and degree of ionization- Freudl really evaluated the impact of polymer rate on mucoadhesion growth. When compared to the control, cationic chitosan HCl demonstrated a noticeable adhesiveness. The mucoadhesive power was greatly increased by the addition of EDTA, an anionic compound. Therefore, anion>cation>non-ionic can be used to explain the mucoadhesive power.

5) Optimum hydration- excessive hydration effects in decreased mucoadhesive power due to formation of a slippery mucilage.

6) Optimum pH - Mucoadhesion is most effective at low pH levels, but at higher pH levels, an extrade inside the conformation transforms the area into a rod-like form, increasing the availability of those for interdiffusion and

interpenetration. Absolute charged polymers, such as chitosan, form polyelectrolyte complexes with mucus at extremely high pH levels and display potent mucoadhesive forces. [21]

Classification of Mucoadhesive Polymer



Flow chart 3- Classification of Polymer

Based on origin of source

1.Natural Polymer – Polymers which can be isolated from natural materials are known as natural polymers. E.g.: Cotton, silk, wool, rubber.

2.Synthetic Polymer – Polymers which can be synthesized from low molecular weight compounds are known as Synthetic Polymers. E.g.: Polyethylene, nylon, terylene.

3.Semisynthetic Polymers – These polymers are frequently created by chemically modifying conspicuous polymers. E.g.: Rayon. [22]

Based on structure

1.Linear Polymer: Molecules form prolonged chains not having branches.

2.Branched Polymer : Molecules which have branch elements that be part of 3 or more segments.

3.Cross-Linked Polymer: It consist of interconnections amongst chains.[23]

Based on molecular force

1.Elastomer: It is a polymer with very inclined intermolecular forces and Viscoelasticity. Therefore they're famously called as elastic polymers.E.g. Natural rubber Polyurethanes, Silicone, Neoprene.

2.Fibers: Any thing that can be woven or otherwise properly formed into a material is referred to as a "fibre". It may be believed that a fibre is a flexible, hair-like strand that is very small in diameter and near to its period, or that a fibre is the smallest visible unit of material synthesis.

3.Thermoplastic: All the plastic materials which can be melted and softened via heating, but they set yet again even as cool are called thermoplastics.

4.Thermosetting polymer: Thermosetting plastics are polymers with low molecular weights that have a semi-fluid character. They begin to skip-link between polymer chains when heated, making them tough and infusible. On the heat-generating software, they create a three-dimensional form. The nature of this reaction is irreversible. The most widely used type of thermosetting polymer is Bakelite, which is used to create electrical insulation.

Based on mode of Polymerization

1.Additional Polymerization: The delivery of monomers of the same type happens immediately. It is a quick chain reaction that has been chemically triggered. Each response sets the stage for a few alternative courses of action. It consists of 3 stages:

Initiation (Birth)

Propagation (Growth)

Termination (Death)

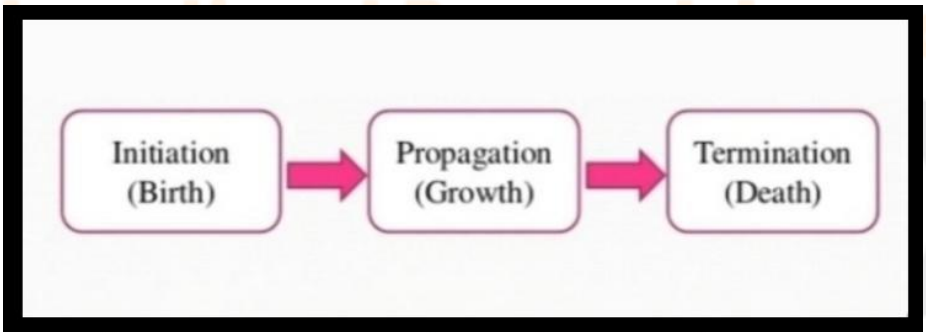
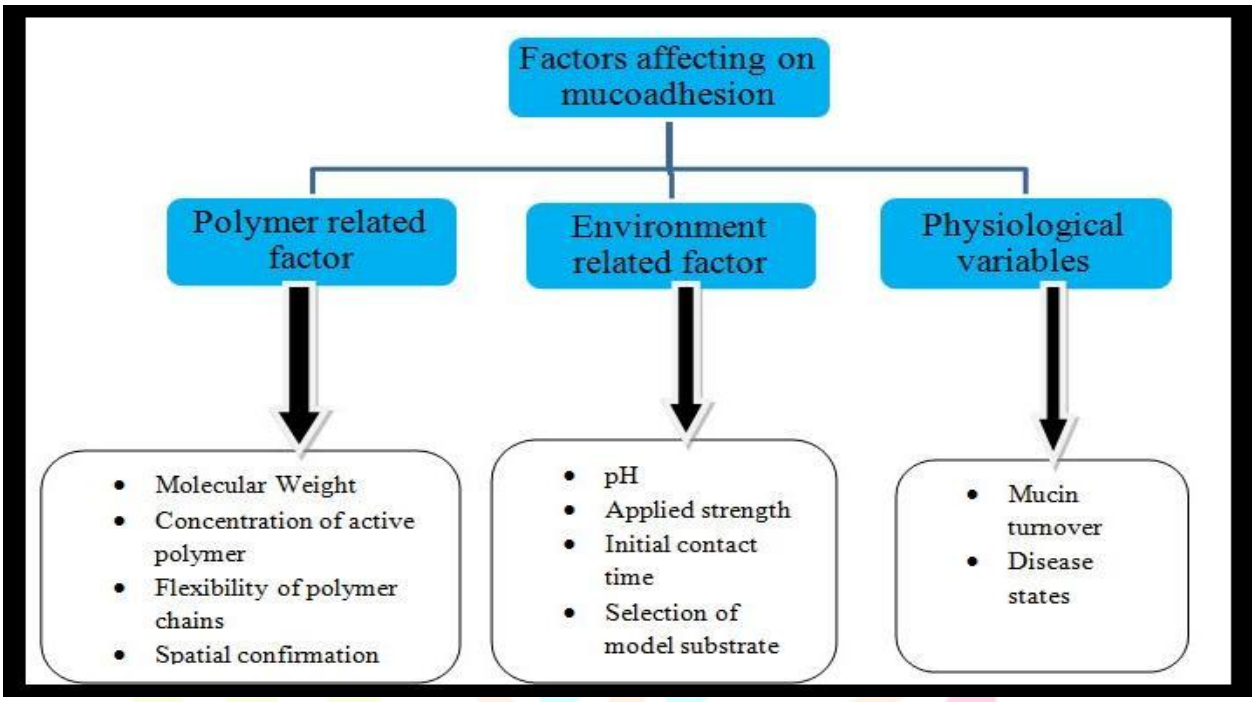


Figure No 8 : Additional Polymerization Stages

2.Condensation Polymerization: It entails the polymerization of monomers together, with the emission of a smooth vial product as a byproduct. A+ B- AB+ via simple product.Characteristic chemical reactions between reactive By product is well-known and compressed. More polymerization occurs faster than this process. Need for responsive, logical groups.

Factor Affecting of Mucoadhesive Drug Delivery System



Flow Chart 4 : Factors Affecting Mucoadhesion

A) Polymer related factors

1) Molecular weight- The bio adhesive properties of a linear polymer are now related to its molecular weight. However, in the case of nonlinear polymers, the molecular weight may or may not be a factor in the bio adhesiveness. Successful bioadhesion necessitates a molecular weight of at least 100,000.[24]

2) Concentration of active polymer- The best understanding of the active polymer is necessary. Beyond a positive most outstanding degree, the adhesive electricity exists in remarkably centred system. decreases noticeably as a result of the coiled molecules being cut off from the medium, which limits the length of chain that may be permeated. When the concentration of polymer is very low, the amount of large, penetrating polymer chains per unit of mucous is low, and the interaction between polymers and mucous becomes irregular.

3) Flexibility of polymer chain- The individual polymer chain mobility decreases as a water soluble polymer becomes flow related, which in turn limits the effective chain duration that may penetrate the mucus layer and lowers the mucoadhesive electricity. Viscosity and diffusion coefficient are the foundations of flexibility. Greater diffusion into the mucus network is motivated by higher polymer flexibility.[25]

4) Spatial conformation– Despite having an excessive molecular weight of roughly 2,100,000, dextrin's adhesive power is comparable to that of PEG, whose molecular weight is 100 times less. In comparison to linear polymer conformation, the helical shape may cover several active groups that are involved in adhesion, lowering the polymer's mucoadhesive power.

5) Swelling- Mucoadhesive polymer requires hydration to enlarge and form a proper Macromolecular mesh of desired duration and moreover to spark off mobility with in the polymer chain which will increase theentanglement way amongst polymer and mucin. Swelling is based upon on the Polymer cognizance, ionic electricity and the presence of water.[26]

6) Cross linking density– Three significant and interconnected structural features of a polymer network are the not uncommon place pore duration, the not exceptional place vast range molecular weight of flow related polymers, and the density of flow connecting. Because water diffuses into the polymer network more slowly with a higher flow linking density and smaller pore duration, there is insufficient swelling of the polymer, which leads to less penetration of the polymer into the mucin.

7) Hydrogen bonding capacity- The polymers ought to contain advantageous groups like carboxylic and hydroxyl groups that can create hydrogen bonding. Hydrogen-bonding-capable polymers include polyvinyl alcohol, polyhydroxylated methacrylate, polymethacrylic acid, and all of their co-polymers.

8) Charge- Ionic polymers have consistently better bioadhesive properties than non-ionic polymers. The cationic polymer like chitosan has better mucoadhesive properties in independent or mildly alkaline media.[27]

B) Environmental related

1) pH of polymer substrate interface- pH has an effect on the ground price of every mucus and polymers. The price density of mucus will vary counting on pH, because of version in dissociation of useful agencies on carbohydrate moiety and amino acids of the polypeptide backbone, which might also additionally have an effect on adhesion.[28]

2) Applied electricity- The initial pressure applied to the online mucoadhesive tissue contact site may have an effect on the interpenetration depth. In spite of the fact that they no longer exhibit desirable interactions with mucin, polymers might become mucoadhesive if excessive strain is applied for a long enough period of time.[29]

Three) First point of contact - The bioadhesive electricity is currently proportional to the first point of contact. Additionally, it establishes the degree of swelling and interpolation of polymers. Gastric systems are unable to manage it.[30]

4) Moistening – Moistening allows the mucoadhesive polymer to spread over the ground and create a macromolecular network of sufficient duration for the penetration of polymer and mucin molecules to increase the mobility of polymer chains.[31,32]

5)Presence of steel ions – Combining with charged agencies of polymer and/or mucous can reduce the huge kind of interaction net web sites and the electricity of mucoadhesive bonding.[33,34]

C) Physiological factors

1) Mucin flip over - Regularly occurring high mucin turnover is not advantageous Because:

a. Despite the fact that the polymer has excellent bioadhesive properties, the immoderate mucin turnover limits the residence period of the bioadhesive polymer as it separates from the mucin layer.

b. High mucin turnover may result in soluble mucin molecules, which interact with the polymer before interacting with the mucin layer. As a result, there won't be enough mucoadhesion anymore.

2) Disease state- The physicochemical belongings of mucus may alter during some diseased state, collectively with common region cold, gastric ulcers, ulcerative colitis, bacterial and fungal infections etc.[35]

3) Renewal rate of mucosal cells– Renewal rate of mucosal cells differs considerably on the basis of varieties of mucosa. It limits the staying power of bioadhesive systems on mucosal surfaces.

Advantages of Mucoadhesive drug delivery system

-Due to full-size blood delivery and appropriate blood float rates, there is rapid absorption. - an increase in medication bioavailability as a result of first avoiding skip metabolism.

-prolongs the house time of the dosage shape on the web page of absorption.

-Because of the mucosal surface, there is better patient compliance, easier drug control, and a speedier beginning of action.

- Due to an multiplied house time it complements absorption and therefore the healing efficacy of the drug - Excellent accessibility .

- Drug is blanketed from degradation with inside the acidic surroundings with inside the git.

Disadvantages of mucoadhesive drug delivery

1.Difficult to achieve high drug release rates required for some drugs.

2.Small mucosal surface for contact.

3.Extent & frequency of attachment may cause local irritation.

4.Lack of flexibility of dosage forms.

Application Mucoadhesive Drug Delivery System

1.Targeting of drug at specific web page of motion.

2.Topical porous microspheres.

3.Release of proteins, hormones and peptides over prolonged length of time.

4.Imaging: numerous cells, molecular lines, tissues and organs may be Imaged the use of radio labelled microspheres.

5.Surface changed microspheres.

6.Gene remedy with DNA plasmids and additionally shipping of insulin.

Conclusion

For some medication candidates, the mucoadhesion phenomenon could serve as a substitute for controlled drug delivery methods. There is no question that the oral route is the most preferred and arguably the most challenging route for drug delivery.This review of mucoadhesive drug delivery structures includes programmes from unique perspectives, such as the development of novel mucoadhesives, device design, mucoadhesion processes, and improved penetration. Mucoadhesive drug transport will play a good extra vital role in transferring those molecules with the inflow of a huge broad range of recent drug molecules due to drug development. The buccal mucosa offers many advantages for controlled drug delivery over extended periods of time. This transport device is designed for managed launch applications thanks to the usage of mucoadhesive polymers.

References

1. Chickering DE III,Mathiowitz E. Fundamentals of bioadhesion. 1999. Bioadhesive drug delivery systems- Funda-Mentals, Novel Approches and Development. In: Lehr CM, editor. New York: Marcel Dekker; P.1- 85.

2 .Ahuja A, Khar RK, Ali J. 1997; Mucoadhesive drug delivery systems. Drug Dev Ind Pharm 23: 489- 515.

3.Gandhi S., Pandya P., Umbarkar R., Tambawala T., Shah M. (2011), Mucoadhesive Drug Delivery System- An Unusual Maneuverer for Site Specific Drug Delivery System, Int J of Pharm Sci., 2:132-152

4.Parthasarathi Subramanian, Mucoadhesive Delivery System: A Smart Way to Improve Bioavailability of Nutraceuticals ,foods 2021, 10, 1362.https://doi.org/10.3390/foods10061362

5. Priya Mahajan, Amanpreet Kaur, Gaeta Aggarwal, S.L.Harikumar. January – March 2013, Mucoadhesive Drug delivery systems: A Review International Journal Of Drug Development & Research | Vol.5

6. Reena Sheoran, May- June 2018; Buccal Drug Delivery systems: A Review Int. J. Pharm. Sci. Rev. Res., 50(1), Article No. 07, Pages: 40-46.

7.Areen Ashkar a, Alejandro Sosnik b, Maya Davidovich-Pinhas a,c,*Structured edible lipid-based particle systems for oral drug-delivery. A. Ashkar et al

8.Füsun Acartürk ,2009,3; Mucoadhesive Vaginal Drug Delivery Systems Recent Patents on Drug Delivery & Formulation 193-205.

9. Misbah Ul Haq M, Munaf Ur Razzak M, Arif Uddin M, Nazish A, Shahidulla SM (2021) Rectal Drug Delivery System: Issue 5• 1000219 Clin Pharmacol Biopharm, an Open access journal ISS: 2177- 065X; Volume 10.Page no. 2of 6.

10.Flavia Laffleur, (2021)120994;Bettina Bauer Review Progress in nasal drug delivery systems. International Journal of Pharmaceutics 607

11.Sapna Rawat, Dinesh Sharma, Poonam Joshi;2020,3(1): Ocular drug delivery systems: approaches to improve Ocular bioavailability; IJHCR, 25-33.

12.K.P. Sampath Kumar, Debjit Bhowmik, G. Harish, S. Duraivel, B. Pragathi Kumar; Ocularinsert: J. Pharm. Innov.2013, A novel controlled drug delivery system ; ISSN: 2277- 7695, vol.1 no.12.

13. Astrid subrizi EvaM.del Amo Viktor Korzhikov -Vlakh Tatiana Tennikova Makira Ruponen Arto Urtti[1][1][2] presented. August 2019, Design principles of ocular drug delivery systems: importance of drug payload, release rate, and material properties. Drug Discovery Today Volume 24,Number 8.

14.Bindu M. Boddupalli, Zulkar N. K. Mohammed, Ravinder Nath A.1, David Banji,Oct- Dec 2010 Mucoadhesive drug delivery system: An overview Journal of Advanced Pharmaceutical Technology & Research | Vol 1 | Issue 4

15.Khan Ab et al.,2014:4, Review on Mucoadhesive drug delivery system: novel approaches in Modern era. Journal of pharmaceutical science,128-40.

16.Vinod KR et al. 2012;4: Critical review on mucoadhesive drug delivery systems. Hygeia JD Med, 1-5.

17. Mahajan P et al. 2013;5: Mucoadhesive drug delivery system: a review. International Journal of Drug Development and Research, 11-20.

18.Vivek Kumar P et al. 2014;5(3): Novel Review on Mucoadhesive Drug Delivery System; Int. J. Res. Pharm. Sci., 205 – 215.

19. J Gopal Maher, M Tara, P Narayan. Yadav, A. Patanaik, P. Mishra, Singh Yadav; (2013);96; Development and characterization of cellulose-Polymethacrylate mucoadhesive film for buccal delivery of carvedilol; Carbohydras. Polyp;172-180

20. Miss. Raut Bhairavi B1, Asst. Prof.Ms Shined Sonal2, June 2022,Mucoadhesive Drug Delivery Systems- An Overview International Journal of Research Publication and Reviews, Vol 3, no 6, pp 4353-4363,

21. Tangri P., Madhav N.V.S. (2011), Oral Mucoadhesive Drug Delivery System-A Review, Int. J. Of Biopharma., 2(1):36-46.

22.Robinson J R and Lee V H; Controlled Drug Delivery – Fundamentals and Applications; Marcel Dekker.

23.Jain N K; Controlled and Novel Drug Delivery; CBS publication.

24.Rahamatullah Shaikh TR et al. 2011; 3 ,Mucoadhesive drug delivery systems. J Pharm Bioall Sci, 89-100.

25.Phanindra B et al.2013, Recent advances in mucoadhesive/bioadhesive drug delivery system: A Review. Int J Pharm Med and Bio Sci., 2(1): 68-84.

26.Lalge M et al. 2014 Mucoadhesive Drug Delivery System: A Review. Critical Review in Pharmaceutical Sciences, 3(3): 17-29.

27.Hitanshi Kulinsinh Parmar, Kartik Kirit Pandya, Lalit Jitendrabhai Pardasani, Vibhuti Sanjeev Panchal and Hemal Thakorbhai Tandel*A SYSTEMATIC REVIEW ON MUCOADHESIVE DRUG DELIVERY SYSTEM World Journal of Pharmaceutical Research SJIF Impact Factor 7.523 Volume 6, Issue 9, 337-366. Review Article ISSN 2277– 7105.

28. Smart J. D.2005, The basics and underlying mechanisms of mucoadhesion. Adv. Drug Del. Rev.57(11): 1556-1568.

29.Gandhi RB, Robinson JR.1994, Oral cavity as a site for bioadhesive drug delivery. Adv Drug Deliv Rev; 13: 43-74.

30.C.M. Lehr et al.1993, A surface energy analysis of mucoadhesion. 2. Prediction of mucoadhesive performance by spreading coefficients. Eur J Pharm Sci, 1: 19-30.

31. Andrews G. P et al.2008; Mucoadhesive polymeric platforms for controlled drug delivery. Eur. J. Pharm. Biopharm, 71(3): 505-518.

32. Miller NS et al, 2005;The use of mucoadhesive polymers in buccal drug delivery. Adv. Drug Del Rev;57: 1666-91.

33. Rathee P et al.2011, Gastrointestional Mucoadhesive drug delivery system: A review. Journal Of pharmacy research, 4(5): 1448-1453.

34.Rajput GC et al.2010 Stomach Specific Mucoadhesive Tablets as Controlled Drug Delivery System. International Journal on Pharmaceutical and Biological Research, 1: 30-41.

35. Bhalodia R et al.2010, Buccoadhesive drug delivery systems: A review. Int J Pharm Bio Sci, 6(2): 1-32.