WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A NEW APPROACH TO MUCOADHESIVE DRUG DELIVERY SYSTEM

Mr. PRATIK S. BHADAGE[1*], Miss. VAISHNAVI M. SHARMA[2], MISS. PARNIKA P. RAJPUT[3]

NES's Gangamai College of Pharmacy Nagaon, Dhule.
1 CONTACT NO.:- 7058144758
E-mail: - pratikbhadage08@gmail.com

ABSTRACT :

Currently, drug delivery system designers are interested in the subject of mucoadhesion. The adhesion between two materials, at least one of which has a mucosal surface, is known as mucoadhesion. A mucoadhesive drug delivery system may be made to allow the dosage form to stay longer at the application or absorption site and to make it easier for the dosage form to make close contact with the underlying absorbing surface. Controlling the release of the medication from a dosage form and extending the residence period of the drug at a specific location are particularly helpful in establishing a regulated plasma level of the drug and enhancing bioavailability. Drug molecules that are not soluble in acid or suffer prolonged first-pass metabolism, for example, may benefit from the application of these dosage forms to mucosal surfaces. This article discusses mucoadhesion, mucoadhesive polymers, and their application in the development of various mucoadhesive drug delivery systems for the gastrointestinal tract, nose, eyes, vagina, and rectal regions. Nevertheless, mucoadhesive research is still in its infancy, and further development is required before the idea can be successfully used to controlled medication delivery.

Keywords: Mucoadhesion, Bio adhesion, Mucoadhesive systems, Drugs delivery.

INTRODUCTION :

The oral route has been recognized as the most often used method of administration among all other routes for the systemic distribution of medications via diverse pharmaceutical products of varying dose forms. Because of its many therapeutic benefits, oral controlled dose formulations have been developed during the past thirty years. This method hasn't worked well for medications, though, that are only partially absorbed in the gastrointestinal tract (GIT) or that are partially absorbed in distinct GIT segments. Due to the gastrointestinal tract's comparatively short transit time, which includes the stomach and small intestine, these medications have a limited absorption window. As a result, the medication is administered in nonadsorbing form and the CR-DF has already exited the upper gastrointestinal system in less than 6 hours. gastrointestinal tract's distal portions. This leads to a brief absorption drug administration was exposed to the idea of mucosal adhesive, also known as mucoadhesive, in the early 1980s. Mucoadhesive drug delivery systems are ones that make use of specific water's natural bio adhesion properties. -soluble polymer that becomes sticky when hydrated, making it possible to target a medication or drug delivery system in a specific area of the body for a prolonged amount of time. This allows for both local drug targeting and It leads to enhanced and/or better therapeutic efficacy of the medication by extending the dosage form's residence duration at the site of application or absorption and facilitating close contact between the dosage form and the underlying absorbing surface. In the past several years, numerous For both systemic and local effects, such mucoadhesive drug delivery systems have been designed for the oral, buccal, nasal, gastrointestinal, rectal, and vaginal routes.

MUCOADHESION MECHANISMS

We still don't fully understand how certain macromolecules adhere to the mucous tissue's surface. To establish intimate contact and promote surface contact, the mucoadhesive must spread across the substrate, which will aid in the diffusion of its chains inside the mucus. There are forces of attraction and repulsion; the attraction forces need to be stronger for a mucoadhesive to work. The kind of dose form and method of administration might help with each phase. For instance, the substrate may adsorbe a partly hydrated polymer due to the surface water's attraction. As a result, the contact stage and the consolidation stage are the two stages that often make up the mucoadhesion process . The interaction between the mucoadhesive and the mucous membrane, which causes the formulation to swell and expand and start to develop a strong bond with the mucus layer, is what distinguishes the first phase. As with ophthalmic or vaginal formulations, there are situations when the distribution mechanism is mechanically coupled across the membrane. In other scenarios, such when employing the nasal route, the deposition is encouraged by the organ's aerodynamics to which the system is delivered. In the gastrointestinal tract, however, direct formulation attachment across the mucosal membrane is not achievable. Peristalsis could help this contact, although there isn't much evidence in the literature to support appropriate adhesion. Additionally, there can be an unfavourable oesophageal adhesion. Mucoadhesion in these circumstances can be explained by Brownian motion or peristalsis, which is the movement of organic

fluids inside the organ cavity. As the particle approaches the mucosal surface, it will experience both repelling and attractive forces. The particle needs to overcome this repulsive barrier. The mucoadhesive elements in the consolidation process are activated by moisture (Figure 1). Moisture makes the system more pliable, allowing the mucoadhesive molecules to split apart and create weak hydrogen and van der Waals connections. The two main theories that describe the consolidation process are diffusion theory and dehydration theory. According to the diffusion theory, chain penetration is the mechanism by which the mucoadhesive molecules and the glycoproteins in mucus interact. The mucoadhesive device contains properties that promote both chemical and mechanical interactions in order for this to occur. Examples of molecules that exhibit mucoadhesive features include those containing hydrogen bond building groups (–OH, –COOH), an anionic surface charge, a high molecular weight, flexible chains, and surface-active characteristics that promote their diffusion throughout the mucus layer.

THEORIES OF MUCOADHESION

Despite the lack of a clear understanding of the chemical and physical underpinnings of mucoadhesion, the phenomena may be explained by six traditional hypotheses that were adopted from research on the performance of various materials and polymer-polymer adhesion.

THEORY OF ELECTRONICS

The foundation of electronic theory is the idea that biological and mucoadhesive materials have opposing electrical charges. The creation of a double electronic layer at the interface results from the flow of electrons between the two materials, and the mucoadhesive strength is determined by the forces that attract inside this electronic double layer.

THEORY OF ADSORPTION

The mucoadhesive device sticks to the mucus by secondary chemical interactions, such as hydrogen and van der Waals bonds, electrostatic attraction, or hydrophobic interactions, according to the adsorption hypothesis. For instance, the most common interfacial force in polymers with carboxyl groups is hydrogen bonding. Since a large number of contacts may produce a powerful global adhesion despite the forces' individual weakness, these forces have been regarded as the most significant in the sticky interaction phenomena.

WETTING HYPOTHESIS

The liquid systems that show affinity to the surface in order to spread across it are covered by the wetting theory. The contact angle is one measurement method that may be used to determine this affinity. The basic norm is that affinity increases with decreasing contact angle. For proper spreadability, the contact angle needs to be equal to or nearly equal to zero.

Equation (1) shows how the spreadability coefficient, SAB, may be computed from the difference between the interfacial energy γAB and the surface energies γB and γA.

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

The adhesion effort, or the energy required to adhere, increases with the individual surface energy of the mucus and the device in proportion to the interfacial energy.

THEORY OF DIFFUSION

The interpenetration of mucin and polymer chains to a depth of adequate to form a semi-permanent adhesive connection is described by diffusion theory (Figure 4). The degree of penetration of the polymer chains is thought to increase the adhesive force. The diffusion coefficient, mucoadhesive chain flexibility and type, mobility, and contact duration all affect this penetration rate. The research indicates that a depth of penetration between 0.2 and 0.5 μm is needed to create an effective bioadhesive binding. Equation 3 may be used to measure the depth of polymer and mucin chain interpenetration: $l = (tDb)\ 1/2$

MUCOADHESIVE SUBSTANCE

In the first research to show the use of a mucoadhesive substance, Nagai suggested employing adhesive tablets as a better therapy for stomatitis. Furthermore, once insulin was administered nasally to dogs in the form of bioadhesive powder, there was an increase in the insulin's systemic bioavailability. Following that, absorption boosters for a variety of administration methods have been employed using bioadhesive materials. Previous studies were also conducted using well-known commercially accessible polymers, namely polyacrylic

Initial Production of Mucoadhesive Substances :

These substances are hydrophilic molecules, which can be manufactured or natural, with a variety of organic functionalities that produce hydrogen bonds, such as carboxyl, hydroxyl, and amino groups. These molecules do not stick to one surface more than another. Mucoadhesives were originally used as denture fixers; the most well-known types of these are cellulose derivatives, carbomers, chitosans, and alginates. They can be added to semisolid formulations including gels, ointments, pastes, and suppositories as well as solid formulations like tablets, transdermal adhesives, and microparticles. The three classes of these polymers are cationic, anionic, and nonionic.

Second-generation Materials for Mucoadhesion

Research on innovative mucoadhesive systems employ polymers with several functions. An ideal polymer should be specific to a specific cellular area or site, stimulate endocytosis, be able to incorporate both hydrophilic and lipophilic drugs, exhibit mucoadhesive properties in both solid and liquid forms, inhibit local enzymes or promote absorption, and finally have a broad safety range. Second generation polymers are what these innovative multifunctional mucoadhesive systems are categorised as. Because they bind or attach to particular chemical structures on the cell or mucus surface, they provide an alternative to non-specific bioadhesives. lectins, invasins, fimbrial proteins, antibodies, and compounds created by incorporating thiol groups into previously identified molecules are good examples of these molecules.

Techniques for examining mudahesion

As of yet, no technology has been created expressly to examine mucoadhesion. Although the majority of the tests were modified from other existing methods, they are helpful and essential for identifying the most promising candidates to be mucoadhesives and for clarifying their modes of action.

Ex vivo and in vitro experiments

Because they aid in the investigation of permeation, release, compatibility, mechanical and physical stability, the surface interaction between the formulation and mucous membrane, and the strength of the bioadhesive bond, in vitro and ex vivo tests are crucial to the development of a controlled release bioadhesive system. Numerous delivery routes, including as oral, buccal, periodontal, nasal, gastrointestinal, vaginal, and rectal, can be simulated by these assays. The following lists the most common in vitro and ex vivo tests found in the literature.

Evaluations of mucoadhesive strength

The majority of in vitro/ex vivo techniques reported in the literature are predicated on the measurement of mucoadhesive strength, or the amount of force needed to release the mucoadhesive from the model membrane. Is it feasible to detach the mucoadhesive from the substrate in a different direction find the tensile strengths for rupture, shear, and detachment. The force that is most frequently measured in these tests is rupture tensile strength. Generally, one uses a texture analyzer or a universal testing equipment (Figure 8). This test determines the amount of force required to remove the formulation from a model membrane, which is often the nasal mucus of a pig or the intestinal mucus of a rat. The model membrane can also be a mucin disc. Plotting a force-distance curve using the results will allow one to determine the force required to separate the mucin disc from the formulation's surface, the peak force, the tensile work (the area under the curve during the detachment process), and the deformation to failure. This method is most frequently used to examine solid systems like microspheres,

Rheological Techniques

All of the techniques in this category are in vitro, and they were initially put out by Hassan and Gallo, who macroscopically examined the formulation-mucin interaction using viscosimetric experiments. The mucoadhesion force may be determined from this test by tracking the viscosimetric changes in the system made up of the selected polymer combination and mucin. It is possible to convert the energy of the chemical and physical linkages in the mucin-polymer interaction into mechanical energy or work. The source of the viscosity shift is this work, which causes the macromolecules to reorganise. The contribution of each component may be used to analyse the coefficient of viscosity of a hydrophilic dispersion including mucin and the mucoadhesive polymer.

Imaging Techniques

There is not enough resolution available with optical microscopes to analyse impacts at the molecular level. A resolution at the micro- or nanometric level is required for these kinds of research. A more expansive picture may be obtained using electronic microscopy, however the environmental requirements for submitting the material are not physiological. To prevent alterations brought on by the electronic analysis, the samples, for example, are examined in a vacuum chamber and are typically coated in a metallic layer.These limitations are removed by the relatively recent technology known as atomic force microscopy (AFM), which operates in any environment—in liquids, air, or vacuum. It gets bigger more than 109-fold, providing a three-dimensional picture of the surface and allowing for the visualisation of individual atoms.

Technique for Dropping Liquid Film

Nielsen, Schubert, and Hansen used a method that Rango Rao and Buri outlined, which entails placing the chosen mucosal membrane within a cylindrical stainless steel tube that has been sliced lengthwise. This support is tilted and located inside a cylindrical chamber with a temperature control of 37 ºC. An isotonic solution is pumped through the mucosal membrane and collected in a beaker. In the case of particle systems, the quantity that remains on the mucosal membrane may then be counted with a coulter counter. It is possible to measure the non adhered mucoadhesive in semi-solid liquids using high performance liquid chromatography.

In vivo experiments

The behaviour of mucoadhesive formulations in vivo, particularly in humans, is poorly understood. Using gamma scintigraphy, the gastrointestinal tract's chitosan mucoadhesion in vivo is examined. Gamma scintigraphy minimises radiation exposure to the individuals while enabling instantaneous visualisation of every formulation transit. The research underscored the significance of in vivo investigations, given that while chitosan has an exceptional mucoadhesion ability in vitro, its retention duration at the absorption site inside the human gastrointestinal system was comparatively brief and lacked significant reproducibility. Animals' gastrointestinal transit times can also be assessed non-invasively, using the Without compromising regular operations, release systems may be designed using opaque radioisotopes, and X-rays can be used to track signals.

CONCLUSION

The effective design of innovative mucoadhesive drug delivery systems may benefit from this review of mucoadhesive dosage forms. Mucoadhesive drug delivery systems are useful from a variety of perspectives, such as the creation of new mucoadhesives, device design, mucoadhesion processes, and improved penetration. Mucoadhesive drug delivery will be much more crucial in delivering the plethora of novel therapeutic compounds that drug research is expected to produce.

Numerous features have been the subject of studies on mucoadhesive systems. It's a field in flux, with the aim of creating more "intelligent" polymers and gadgets, as well as developing new approaches to better understand the mucoadhesion phenomena. The creation of novel medications may depend more on mucoadhesive systems due to the massive input of new compounds resulting from pharmacological research.

REFERENCES :

1.Mucoadhesive drug delivery systems: Ahuja A, Khar RK, and Ali J. Ind Pharm Drug Dev. 1997;23(5):489–515.

2. Rheological evaluation of bioadhesive binary polymeric systems intended as drug delivery implant platforms by Andrews GP and Jones DS. (2006) Biomacromol. 7:899-906.

3. Jones DS, Laverty TP, and Andrews GP. Mucoadhesive polymeric platforms for regulated administration of medication. 71(3):505–518 in Eur J Pharm Biopharm. (2008).

4. Grabnar I, Mrhar A, Dimnik AD, Vovk T, Kerec M, and Bocataj M. Zeta potential and mucoadhesion strength on the vesical mucosa of pigs are correlated. Bull Biol Pharm 2003;26(5):743-746.

5. Farabollini A, Bravo-Osuna I, Vauthier C, Palmieri GF, and Ponchel G. The mucoadhesion mechanism of poly(isobutiyl cyanoacrylate) core-shell nanoparticles containing chitosan and thiolated chitosan.Biomaterials, 28(13): 2243–2236, 2007.

6. Bromberg L, Alakhov V, Temchenko M, and Hatton TA.

7. Oral bioadhesive drug delivery methods, Bruschi ML, Freitas O. Drug Ind. Pharm., 31(3), 293–310, 2005.

8. Panzeri H, Gremião MPD, Freitas O, Bruschi ML, Jones DS, and Lara Ehg. Propolis-containing semisolid solutions for the treatment of periodontal disease: syringeability, rheological, textural, mucoadhesive, and in vitro release kinetics. 2007;96(8):2074–2089; J Pharm Sci.

9. Panzeri H, Gremião MPD, Freitas O, Bruschi ML, Jones DS, and Lara Ehg. Creation and characterisation of propolis-containing microparticles as a liquid crystalline phase precursor for periodontal disease therapy. 2008;34(3):267–278; Drug Develop Ind Pharm.

10. Foreman P, Ludwig A, Callens C, Ceulemans J, and Remon JP. Rheological analysis of several nasal powder formulations' mucoadhesivity. In 2003, Eur J Pharm Biopharm, 55(3), 323–328.

11. Ludwig A., Vinckier I., and Ceulemans J. Rheological evaluation of xantan gum's interaction with mucin in an ophthalmic liquid dose form. 2002;91(4):1117–1127; J Pharm Sci.

12. Rao YS and Chowdary CPR. Mucoadhesive microspheres for regulated administration of medication. 2004;27(11):1717–1724; Biol Pharm Bull.

13. Magner E, Bromberg L, and Cleary J. The adhesion of polyacrylic acid modified with polyether to mucin. 2004;20(22):9755–9762 Langmuir.

14. Gremião MPD, Oliveira AG, Silva Junior AA, Urban MCC, and Formariz TP. Como sistemas de liberação de fármacos, microemulsões e fases líquidas cristalinas são utilizadas. 2005;41(3):301-313; Rev Bras Ciênc Farm.

15. Goto T, Takayama K, Morishita M, Kavimandan NJ, and Peppas NA. Rats' mucoadhesive properties and intestinal transit using complexation

hydrogels. (2006) J Pharm Sci;95(2):462-469.
16. Bernkop-Schnürch, Guggi D, and Grabovac V17. Mathiowitz E, Chickering DE, III. Basics of bioadhesion. Editor: Lehr, CM. The basics, innovative methods, and development of bioadhesive drug delivery systems. Marcel Dekker, New York, 1999, pp. 1–85. [Scholar Google]
18. Mucoadhesive drug delivery methods, Ahuja A, Khar RK, Ali J. 1997;23:489–515, Drug Dev Ind Pharm. [Scholar Google]
19. Veuillez F, Buri P, Deshusses J, Jacques Y, Kalia YN. Components and methods for enhancing peptide absorption through the buccal mucosa. In 2001, Eur J Pharm Biopharm, 51:93–109. [PubMed] [Scholar Google]
20.Polymers in mucoadhesive buccal drug delivery systems: A review, Punitha S, Girish Y. (2010) Int J Res Pharm Sci;1:170–86. [Scholar Google]
21.Smart JD: The fundamentals and underlying processes of mucoadhesion. Pharmacotherapy Advances. 2005;57:1556–1568. [PubMed] [Scholar Google] 22. Sultana Y, Aqil M, Ali A. Ocular inserts for pefloxacin mesylate regulated delivery: preparation and assessment. Acta Pharm. 2005;55(3):307–14. [PubMed] [Scholar Google]
23. Samanta MK, Wagh VD, and Inamdar B. Polymers utilised in medication delivery systems and ocular dosage forms. 2008;2:12–7; Asian J Pharmaceutics. [Scholar Google]
24. Taha RA, Elhadi SS, Mortada ND, Awad GA, and Zaki NM. creation of a mucoadhesive mebeverine hydrochloride solution and in situ gelling for rectal administration. Pharm J Saudi Arabia 2003;11:150–71. [Scholar Google]
25. Amaral MH, Bahia MF, and Neves JD. medication distribution via vagina. In: Editor Gad SC. New Jersey: John Willey and Sons Inc., 2007. Pharmaceutical Manufacturing Handbook, pp. 809–78. [Scholar Google]
26. Choi HG, Kim CK. Enhanced absorption of acetaminophen-containing mucoadhesive liquid suppository and in situ gelling. 165:23–32; Int J Pharm. 1998.

27.Asane GS. Overview of mucoadhesive gastro intestinal medication delivery system. 2007;5:1–5. Pharmainfo.net. [Scholar Google]
28. Schnürch AB. Oral medication administration using mucoadhesive systems. 2005;2:83–7; Drug Discov Today Technol. [PubMed] [Scholar Google]
29. Tucker G, Drummond BK, Rathbone MJ. The mouth as a delivery route for systemic medications. Drug Deliv Rev. Adv. 1994;13:1-22. [Scholar Google]
30. Thakor RS, Patel BP, Majmudar FD, Patel JK, Patel KN, Rajput GC, et al. Review of the literature on stomach-specific mucoadhesive tablets as a regulated medication delivery mechanism. (2010) Int J Pharm Biol Res;1:30–41. [Scholar Google]
31. Kailas M, Sfurti S, Remeth D. Acyclovir mucoadhesive tablet absorption investigations conducted in vitro. 2010;44:183–8 Indian J Pharm Educ Res. [Scholar Google]
32. The formulation of a water-soluble mucoadhesive film containing lycopene for the treatment of leukoplakia was carried out by Shah D, Gaud RS, Misra AN, and Parikh R. 2010;12:6–11. Int J Pharm Sci Rev Res. [Scholar Google]
33. Pimozide buccal mucoadhesive patch formulation and assessment, Biswajit B, Kevin G, Thimmasetty J. Nanotechnology in J Pharm Sci Int. 2010;2:32–41. [Scholar Google]
34. Creation and assessment of controlled release Eudragit buccal patches: Wong CF, Yuen KH, Peh KK. Int J Pharm. 1999;178:11–22. [Google Scholar] [PubMed]
35. Haglund BO, Himmelstein KJ, Kumar S. In situ-forming gels for the administration of medications to the eyes. J Ocul Pharmacol. 1994;10:47–56. [Google Scholar] [PubMed]
36. A very viscous gel ointment containing carbopol for use on the oral mucosa was developed by Ishida M, Nambu N, and Nagai T. Bull Chem Pharm. 1983;31:4561–4. [Google Scholar] [PubMed]