



AMERICAN JOURNAL OF PHARMTECH RESEARCH

Mucoadhesive Drug Delivery System: A Review

D.D. Chechare*, M. Siddaiah

Department of Pharmaceutical Sciences, Bhagwant University, Rajasthan, India.

ABSTRACT

Mucoadhesive drug delivery systems interact with the mucus layer covering the mucosal epithelial surface, and mucin molecules and increase the residence time of the dosage form at the site of absorption. The drugs which have local action or those which have maximum absorption in gastrointestinal tract (GIT) require increased duration of stay in GIT. Thus, mucoadhesive dosage forms are advantageous in increasing the drug plasma concentrations and also therapeutic activity. In this regard, this review covers the areas of mechanisms, polymers used in mucoadhesion, factors influencing the mucoadhesive and also various mucoadhesive dosage forms.

Keywords: Mucoadhesion, theories, mucoadhesive dosage forms.

*Corresponding Author Email: dheerajchechare7@gmail.com

Received 08 September 2018, Accepted 18 October 2018

Please cite this article as: Chechare DD *et al.*, Mucoadhesive Drug Delivery System: A Review. American Journal of PharmTech Research 2018.

INTRODUCTION

The term bioadhesion implies attachment of a drug carrier system to a specific biological location. The biological surface can be epithelial tissue. If adhesive attachment is to a mucus coat, the phenomenon is referred to as mucoadhesion.⁽¹⁾ Mucoadhesive drug delivery systems prolong the residence time of the dosage form at the site of application or absorption. They facilitate an intimate contact of the dosage form with the underlying absorption surface and thus improve the therapeutic performance of the drug. In recent years, many such mucoadhesive drug delivery systems have been developed for oral, buccal, nasal, rectal and vaginal routes for both systemic and local effects.⁽²⁾ Dosage forms designed for mucoadhesive drug delivery should be small and flexible enough to be acceptable for patients and should not cause irritation. Other desired characteristics of a mucoadhesive dosage form include high drug loading capacity, controlled drug release (preferably unidirectional release), good mucoadhesive properties, smooth surface, tastelessness, and convenient application. Erodible formulations can be beneficial because they do not require system retrieval at the end of desired dosing interval. A number of relevant mucoadhesive dosage forms have been developed for a variety of drugs. Several peptides, including thyrotropin-releasing hormone (TRH), insulin, octreotide, leuprolide, and oxytocin, have been delivered via the mucosal route, albeit with relatively low bioavailability (0.1–5%), owing to their hydrophilicity and large molecular weight, as well as the inherent permeation and enzymatic barriers of the mucosa. The development of sustain release dosage form can achieve the aim of releasing the drug slowly for a long period but this is not sufficient to get sustained therapeutic effect. They may be cleared from the site of absorption before emptying the drug content. Instead, the mucoadhesive dosage form will serve both the purposes of sustain release and presence of dosage form at the site of absorption. In this regard, our review is high lighting few aspects of mucoadhesive drug delivery systems.⁽³⁾

Mechanism of Mucoadhesion

Mucoadhesion is complex phenomenon which allows attachment of drug molecule to the mucous layer with the aid of suitable carrier. Mucoadhesion process consists of various actions such as wetting, adsorption and interpenetration of polymer chains. Numbers of steps have been involved in the process of mucoadhesive bond formation. The first step of mucoadhesion process involves spreading, wetting, and dissolution of polymeric chain at the interface. Next step of mucoadhesion is interpenetration layer in which mechanical or physical entanglement between polymeric materials with the surface of mucosal layer occurs. The last step involves chemical interactions (hydrogen bonding, covalent bonding, ionic bonds, and Van der Waals' interactions).⁽⁴⁾

Advantages of Oral Mucoadhesive Drug Delivery Systems

- 1) Prolongs the residence time of the dosage form at the site of absorption hence increases the bioavailability.
- 2) Rapid onset of action.
- 3) Reduction in dosing frequency.
- 4) Drug is protected from degradation in the acidic environment in the GIT.
- 5) Improved patient compliance.⁽⁵⁾

Disadvantages Of Mucoadhesive Drug Delivery Systems

- 1) Occurrence of local ulcerous effects due to prolonged contact of the drug possessing ulcerogenic property.
- 2) One of the major limitations in the development of oral mucosal delivery is the lack of a good model for in vitro screening to identify drugs suitable for such administration.
- 3) Patient acceptability in terms to taste, irritancy and mouth feel is to be checked.⁽⁵⁾

Polymers Used For Mucoadhesive Drug Delivery

These polymers are classified as:

Hydrophilic polymers:

Contains carboxylic group and possess excellent mucoadhesive properties. These are,

- PVP (Poly vinyl pyrrolidine)
- MC (Methyl cellulose)
- SCMC (Sodium carboxyl methyl cellulose)
- HPC (Hydroxyl propyl cellulose)

Hydrogels

These swell when in contact with water and adhere to the mucus membrane. These are further classified according to their charge

Anionic polymers - carbopol, polyacrylates

Cationic polymers - chitosan

Neural/ non-ionic polymers - eudragit analogues⁽⁶⁾

Factors Affecting Mucoadhesion

Molecular weight

The mucoadhesive strength of a polymer increases with molecular weights above 100,000. Direct correlation between the mucoadhesive strength of polyoxyethylene polymers and their molecular weights lies in the range of 2,00,000–70,00,000.⁽⁷⁾

Flexibility

Mucoadhesion starts with the diffusion of the polymer chains in the interfacial region. Therefore, it is important that the polymer chains contain a substantial degree of flexibility in order to achieve the desired entanglement with the mucus. The increased chain interpenetration was attributed to the increased structural flexibility of the polymer upon incorporation of polyethylene glycol. In general, mobility and flexibility of polymers can be related to their viscosities and diffusion coefficients, as higher flexibility of a polymer causes greater diffusion into the mucus network.⁽⁸⁾

Cross-linking density

The average pore size, the number and average molecular weight of the cross-linked polymers, and the density of cross-linking are three important and inter-related structural parameters of a polymer network. Therefore, it seems reasonable that with increasing density of crosslinking, diffusion of water into the polymer network occurs at a lower rate which, in turn, causes an insufficient swelling of the polymer and a decreased rate of interpenetration between polymer and mucin.⁽⁹⁾

Hydrogen bonding capacity

Hydrogen bonding is another important factor in mucoadhesion of a polymer. Desired polymers must have functional groups that are able to form hydrogen bonds, and flexibility of the polymer is important to improve this hydrogen bonding potential. Polymers such as poly(vinyl alcohol), hydroxylated methacrylate, and poly(methacrylic acid), as well as all their copolymers, have good hydrogen bonding capacity.⁽¹⁰⁾

Hydration

Hydration is required for a mucoadhesive polymer to expand and create a proper macromolecular mesh of sufficient size, and also to induce mobility in the polymer chains in order to enhance the interpenetration process between polymer and mucin. Polymer swelling permits a mechanical entanglement by exposing the bioadhesive sites for hydrogen bonding and/or electrostatic interaction between the polymer and the mucus network. However, a critical degree of hydration of the mucoadhesive polymer exists where optimum swelling and mucoadhesion occurs.⁽¹⁰⁾

Charge

Some generalizations about the charge of bioadhesive polymers have been made previously, where nonionic polymers appear to undergo a smaller degree of adhesion compared to anionic polymers. Strong anionic charge on the polymer is one of the required characteristics for mucoadhesion. Some cationic polymers are likely to demonstrate superior mucoadhesive properties, especially in a neutral or slightly alkaline medium. Additionally, some cationic high-molecular-weight polymers, such as chitosan, have shown to possess good adhesive properties. There is no significant literature about

the influence of the charge of the membrane on the mucoadhesion but the pH of the membrane affects the mucoadhesion as it can influence the ionized or un-ionized forms of the polymers.⁽¹¹⁾

Mucoadhesive Dosage Form

Tablets

Tablets are small, flat and oval, with a diameter of approximately 5–8 mm. Unlike the conventional tablets, mucoadhesive tablets allow for drinking and speaking without major discomfort. They soften, adhere to the mucosa, and are retained in position until dissolution and/or release is complete. Mucoadhesive tablets, in general, have the potential to be used for controlled release drug delivery, but coupling of mucoadhesive properties to tablet has additional advantages, for example, it offers efficient absorption and enhanced bioavailability of the drugs due to a high surface to volume ratio and facilitates a much more intimate contact with the mucus layer. This mucoadhesive tablet allowed patients to eat and speak without discomfort and caused no irritation, bad taste or pain.⁽¹²⁾

Patches

Several different patch systems that adhere to the oral mucosa and are designed to deliver drugs have been developed. There are basically three different types of oro-adhesive patches: patches with a dissolvable matrix for drug delivery to the oral cavity. These patches are longer acting than solid forms such as tablets and lozenges and can produce sustained drug release for treating oral candidiasis and mucositis.⁽¹³⁾

Films

Mucoadhesive films may be preferred over adhesive tablets in terms of flexibility and comfort. In addition, they can circumvent the relatively short residence time of oral gels on the mucosa, which are easily washed away and removed by saliva. Thin strips of polymeric films, capable of loading up to 20 mg of drugs, dissolve on the tongue in less than 30 s and deliver drugs (which are able to cross the permeability barrier) directly to the blood supply for rapid treatment of conditions such as impotence, migraines, motion sickness, pain relief and nausea.⁽¹⁴⁾

Gels and ointments

Semisolid dosage forms, such as gels and ointments, have the advantage of easy dispersion throughout the oral mucosa. However, drug dosing from semisolid dosage forms may not be as accurate as from tablets, patches, or films. Poor retention of the gels at the site of application has been overcome by using mucoadhesive formulations. Certain mucoadhesive polymers, for example, sodium carboxymethylcellulose, carbopol, hyaluronic acid, and xanthan gum, undergo a phase change from liquid to semisolid. This change enhances the viscosity, which results in sustained and

controlled release of drugs. Hydrogels are also a promising dosage form for buccal drug delivery. Gels applied to the oral mucosa have been trialled for the delivery of systemic analgesics, antihypertensive and drugs for treating cardiovascular disease as well as topical delivery of antifungal agents, anti-inflammatories and mucoprotective agents to the oral mucosa.⁽¹⁵⁾

Sprays

Spray which is capable of delivering large molecules, such as insulin across the oral mucosa. Glyceryltrinitrate is a small molecule that can be rapidly delivered across the sublingual oral mucosa using a spray for angina relief.⁽¹⁶⁾

Pastes

Pastes have been utilized in the delivery of antimicrobial agents for improved extraction socket healing after tooth extractions in patients with HIV disease and for the delivery of controlled release triclosan in oral care formulations. Pastes are also being used for the local delivery and retention of slow release minocycline in the gingival crevice surrounding teeth in the treatment of periodontal disease. Liposomes have been investigated as drug delivery carriers both as a solution and in a paste formulation.⁽¹⁷⁾

CONCLUSION

Mucoadhesive systems are known to provide intimate contact between dosage form and the absorptive mucosa, resulting thereby in a high drug flux through the absorbing tissue. Studies on mucoadhesive systems have focused on a broad array of aspects. It is a growth area whose goal is the development of new devices and more “intelligent” polymers, as well as the creation of new methodologies that can better elucidate the mucoadhesion phenomenon. With the appropriate technologies, delivery techniques and the choice of the polymer for the oral mucosa could, in the future, be utilized for the treatment of many diseases both mucosal and systemic and the catalogue of drugs which can be delivered via the mucosa could be greatly increased.

REFERENCES

1. Miller N, Chittchang M and Johnston T. The Use of Mucoadhesive Polymers in Buccal Drug Delivery, *Advanced Drug Delivery Reviews*, 2005; 57: 1666-1691.
2. Ahuja A, Khar RK, Ali J. Mucoadhesive drug delivery systems. *Drug Dev Ind Pharm* 1997;23:489-515.
3. Veuillez F, Kalia YN, Jacques Y, Deshusses J, Buri P. Factors and strategies for improving buccal absorption of peptides. *Eur J Pharm Biopharm* 2001;51:93-109.
4. Mathew AK. Oral local drug delivery: An overview. *Pharm Pharmacol Res.* 2015;3(1):1-6.

5. G.S. Asane, mucoadhesive gastro intestinal drug delivery system: an overview, 2007; 5(6).
6. Andrews G.P., Lavery T.P., Jones D.S., Mucoadhesive polymeric platforms for controlled drug delivery, Eur. J. Pharm. Biopharm., 2009; 71: 505–518.
7. Tiwari D, Goldman D, Sause R, Madan PL. Evaluation of polyoxyethylene homopolymers for buccal bioadhesive drug delivery device formulations. AAPS Pharm Sci 1999;1:13-21.
8. Huang Y, Leobandung W, Foss A, Peppas NA. Molecular aspects of muco- and bioadhesion: Tethered structures and site-specific surfaces. J Control Release 2000;65:63-71.
9. Gu JM, Robinson JR, Leung SH. Binding of acrylic polymers to mucin/epithelial surfaces: Structure–property relationships. Crit Rev Ther Drug Carrier Syst 1998;5:21-67.
10. Peppas NA, Buri PA. Surface, interfacial and molecular aspects of polymer bioadhesion on soft tissues. J Control Release 1985;2:257- 75.
11. Smart JD, Mortazavi SA. An investigation of the pH within the hydrating gel layer of a poly(acrylic acid) compact. J Pharm Pharmacol 1995;47:1099.
12. Rajput GC, Majmudar FD, Patel JK, Patel KN, Thakor RS, Patel BP, et al. Stomach specific mucoadhesive tablets as controlled drug delivery system: A review work. Int J Pharm Biol Res. 2010; 1: 30–41.
13. Gibson J, Halliday J A, Ewert K and Robertson S “A Controlled Release Pilocarpine Buccal Insert In The Treatment of Sjogren’s Syndrome”, Br. Dent. J., 2007; 202(8): E17–E17.
14. Shah D, Gaud RS, Misra AN, Parikh R. Formulation of a water soluble mucoadhesive film of lycopene for treatment of leukoplakia. Int J Pharm Sci Rev Res., 2010; 12: 6–11.
15. Martin L, Wilson CG, Koosha F, Uchegbu IF. Sustained buccal delivery of the hydrophobic drug denbufylline using physically cross-linked palmitoyl glycol chitosan hydrogels. Eur J Pharm Biopharm., 2003; 55: 35–45.
16. Intel Genx Corp. (2006), Quick Release Wafer Technology, VERSAFILM, Intelgenx Corp.
17. Palermo A, Napoli N, Manfrini S, Lauria A, Stollo R and Pozzilli P “Buccal Spray Insulin In Subjects With Impaired Glucose Tolerance: The Prevoral Study”, Diab. Obes. Metab., 2011; 13: 42-46.

AJPTR is

- Peer-reviewed
- bimonthly
- Rapid publication

Submit your manuscript at: editor@ajptr.com

