Mucoadhesive drug delivery system: an overview

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ABSTRACT
The major objective of any dosage form is to deliver an optimum therapeutic amount of active agent to the proper site in the body to attain constant & maintenance of the desired drug concentration. Mucoadhesive drug delivery systems are effective delivery systems with various advantages as compared to other oral controlled release dosage forms in terms of drug delivery at specific sites with prolonged retention time of drugs at target sites. The main advantage of these systems includes avoiding first pass metabolism of the drugs and hence availability of high drug concentration at target site. Oral mucoadhesive systems have potential ability for controlled and extended release profile so as to get better performance and patient compliance. The present manuscript briefly reviews the benefits of mucoadhesive drug delivery systems, mechanisms involved in mucoadhesion, different factors affecting mucoadhesive drug delivery systems.

Keywords: Oral route, Mucoadhesive drug delivery system, Bioavailability

Introduction
The research and development in drug delivery of active agents has made major contribution in the pharmaceutical industry and significantly provided a vital role in treatment of diseases, thereby constantly improving the quality of life. Among all other routes of drug administration, oral route is most preferable route of administration because of high patient acceptance rate with wider advantages (easy administration, pain avoidance, accurate dosing, cost effective with flexibility in manufacturing methods and versatility.¹ The approach of mucoadhesive drug delivery system had been arised in early 1980. Adhesion can be defined as bond formation between a pressure sensitive adhesive and a surface. Mucoadhesion is bond formation between pressure sensitive adhesive with biological substrate (mucosal layer).²,³ In design and development of drug delivery systems mucoadhesive drug delivery has been considered as subject of great interest due to various merits. Prolongation of the residence time of the dosage form at the site of application by increasing intimate contact of the dosage form with the underlying absorption surface and leads to improved absorption properties with enhanced bioavailability of therapeutic agents is major quality of these systems. Localization of the active ingredients for therapeutic effect at specific site in the body makes mucoadhesive controlled drug delivery systems more beneficial leads to controlled and predictable drug release from the dosage form and make them potential candidate for treatment of different diseases.⁴ Different factors (characteristics of mucosal membrane and the physicochemical properties

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of used polymers) play major contributing role in better efficiency of these drug carriers. Various mucosal routes for drug delivery includes buccal/oral route, nasal route, ocular route, vaginal route and gastrointestinal route. This review article provides brief overview of the mucoadhesion, various advantages and factors affecting mucoadhesion.

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.

Advantages of mucoadhesion

Mucoadhesive drug delivery system has several benefits which are as follows:
- Improved bioavailability by prolongation of the residence time of the dosage form at the site of absorption
- Excellent accessibility
- Rapid onset of action possible
- Good perfusion rates promotes rapid absorption of dosage form
- Some drugs are degraded in the acidic environment of the GIT these systems are better alternative to such drugs
- Better patient compliance-ease of drug administration
- Rapid healing of the local site
- Reduction in dosing frequency
- Better control over plasma levels in these dosage forms increases the safety margin of highly potent active drug moieties drugs enables reduction in total quantity of drug administration
- Surface of mucosal layer provides fast onset of action
- Some drugs which are degraded by enzymatic or alkaline environment of stomach and intestine can be administered by mucosal route effectively. *e.g.* Buccal sublingual
- The mucosal layer has higher perfusion rate with blood vessels and higher permeation rate than the skin.

Factors affecting mucoadhesion

Polymer related factors

*Molecular weight*

Mucoadhesive property of the polymer increases with increase in molecular weight of polymeric chain.

*Chain length*

As chain length of the polymeric materials increases mucoadhesiveness also increases.

*Spatial arrangement*

Along with different material related factors (weight and length of polymer) spatial arrangements or confirmation of a molecule is another necessary factor for mucoadhesive property. A very good example for this is dextran in which helical structure of dextran may enclose many active groups of adhesive property, unlike poly ethylene glycol polymer which possess a linear structural confirmation.

*Flexibility*

Flexible nature of polymer is another important parameter for mucoadhesive property because chain length of polymer facilitates good penetration and attachment of the polymer chains with mucosal lining of the biological membrane and helps in improvement of bioadhesive property. The flexibility of the polymer chains is generally affected by
hydration and cross linking reactions of the polymer network. If cross linking density of the polymer is high flexibility of the polymeric chains is low.\(^4\)

**Hydration of polymer**

A polymeric material of reduced flexibility, with high cross linking reduces the diffusion of water into the cross linked chains of polymer. Therefore highly cross linked polymeric materials restricts the interpenetration of polymer and mucin of the mucosal layer leads to decrease in mucoadhesive ability.\(^11\)

**Hydrogen bonding**

Adhesion of polymers is greatly depend upon the hydrogen bonding that higher the hydrogen bonding stronger is the adhesive strength of the polymers. Main functional groups responsible for such type of interactions are hydroxyl, carboxyl and amino groups.\(^12\)

**Charge and degree of ionization of polymer**

Neutral polymeric materials have less adhesive property as compared to anionic polyelectrolytes which have good bioadhesion because presence of charge functional groups in the polymeric chains has a marked effect on the strength of the bioadhesion.\(^13\)

**Polymer concentration**

Concentration of polymers also affects the adhesive strength and mucoadhesion with mucosal layer. Polymer concentration in the range of 1-2.5 wt% may show significant mucoadhesive ability for biomedical purposes.\(^14\)

**Environmental factors**

In addition to various physicochemical factors of the polymeric materials that significantly affect the effectiveness of mucoadhesive drug delivery systems, different environmental factors also contribute an important part in mucoadhesion property.\(^15\)

**pH**

Different studies have been conducted to explore effectiveness of these systems and clearly indicated that the degree of hydration of cross linking is strongly affected by pH of the medium.\(^6,16,17\)

**Applied strength**

The depth of interpenetration between mucoadhesive system and mucosal tissue layer is depends upon the degree of pressure application. Polymeric materials used for mucoadhesion may become more mucoadhesive even though they do not have good interaction with mucin if these materials are applied with high pressure for longer period of time.

**Contact time**

With the initial increase in the contact time there is an increase in the hydration of the polymer matrix and subsequent interpenetration of the polymer chains. The physiology of the mucosal layer may vary depending on the pathophysiological.\(^2,18\)

**Swelling**

Concentration and hydrating properties of polymer used have significant effect on swelling and bioadhesion is decreases if polymeric materials have high swelling index.

**Physiological factors**

In addition to physic chemical factors physiological factors also play very essential role in the mucoadhesive ability of a polymer matrix include texture and thickness of mucosa.\(^17\)

**Mucin turnover**

The mucin turnover is expected to limit the residence time of the mucoadhesive on the mucus layer. No matter how high the mucoadhesive strength is.\(^19\)

**Disease state**

There are various diseases conditions which change the physicochemical characteristics of the mucus such as common cold, gastric ulcers, ulcerative colitis, etc. which directly affects the mucoadhesion effectiveness.\(^20\)
Conclusions

Mucoadhesion have great pharmaceutical applications and this phenomenon can serve as a good approach in the area of controlled drug delivery systems for a number of active drug molecules. These drug delivery systems with significant advantages including prolonged retention time of the drugs which directly affects the absorption rates are key factors in the oral bioavailability of various drugs. Many potential mucoadhesive systems with different rate controlling agents are being explored which may results into better treatment approach in the market in near future and provide effective healthcare benefits to the community.

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References
