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CRITICAL REVIEW ON RECENT ADVANCES IN MUCOADHESIVE DRUG DELIVERY SYSTEM

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ABSTRACT
These articles include polymers used in mucosal delivery of therapeutic agent. Novel drug delivery methods come under the mucoadhesive drug delivery system because the porous nature of mucus membrane which allow the uptake of drug into systemic circulation and avoids the first pass metabolism.[5] Mucoadhesion phenomenon which involves wetting, adsorption and interpenetration of polymer chains. These review article provides the information about mucoadhesion, mucoadhesive polymers, factor affecting mucoadhesion, evaluation parameter and mucoadhesive drug delivery systems.[4,5]

KEYWORDS- Mucoadhesion, Bioadhesion, Mucoadhesive Polymers, Mechanism, Theories, Evaluation.

INTRODUCTION
The adhesion may be defined as the molecular force of attraction in the area of contact between pressure sensitive adhesive and a surface. The bioadhesion means bond formation between biological and synthetic surface. Bioadhesion used to study adhesion between polymer (synthetic or natural), gastrointestinal mucosal membrane and soft tissues. If some times the bond formation takes place with mucus the term mucoadhesion may be used.[6]

Oral delivery is the commonly use route of administration because ease to administration, accurate dosing, less cost and more stability.[4,10] Generally oral delivery product shows improved shelf life. Mucoadhesion may be preferred as a state in which two components, in which one is biological nature are held together for prolonged period because of interfacial forces.[7]

Mucoadhesive drug delivery has been interesting topic to growing to development in the design of drug delivery system used to improve the extended period of dosage form at the site of application and to facilitate the intimate contact of formation. So, it improves the bioavailability of formulation.[7,8,9] Mucoadhesive drug delivery systems are useful which gives a controlled drug release over a period.

Mucoadhesive /Bioadhesive drug delivery system contains the following.[7]

1. Buccal delivery system
2. Oral delivery system
3. Vaginal delivery system
4. Rectal delivery system
5. Ocular delivery system
6. Nasal delivery system

Examples-Several peptides, including thyrotropin releasing hormone (TRH), octreotide, insulin, leuprolide and oxytocin delivered through mucosal membrane. They should be small, it could be acceptable for patients and not causes irritation.[4,5]

Mucous Membrane
Mucous membrane are the moist surfaces, lining the walls of various body cavities such as respiratory and gastrointestinal tract. Mostly they are consisting of connective tissue above is an epithelial layer, upper part is moist because the presence of mucous membrane.[5,6] Epithelia may be either single layered (e.g. stomach, small and large intestine and bronchi) or multilayered (e.g. esophagus, vagina and cornea).[5]

The former contains goblet cells which secrete mucus directly on the epithelial surfaces, latter contain adjacent to tissues containing specialized glands such as salivary glands secrete mucus on epithelial surface. Mucus found as gel layer adhere to mucosal surface or as a soluble.[1,4]

Mostly mucus gel contains mucin glycoproteins, lipids, inorganic salts and water after comparing of its weight, making it highly hydrated system. Mucin glycoproteins which provide mucus with its characteristics gel like, cohesive and adhesive properties.[2] Mucus layer having a thickness 50 to 450µm in the stomach, to less than 1

µm in oral route. Protection and lubrication is the major function of mucus.[4]

Composition of mucus layer

Mucus forms thin gel layer sticking to the mucosal epithelial surface.Mucin glycoproteins having high molecular weight proteins having oligosaccharide units. e.g. Sialic acid, L-fructose etc.[5]

Function of mucous layer[5,6,8]

1. It is protective layer because of hydrophobicity.
2. The epithelial cell surface contains a gel layer which is strongly bonded to each other.
3. It maintains the lubrication of mucosal membrane which help to maintain the moisture.

Mucoadhesion and bioadhesion[4,6,8]

In the early 1980s the concept of mucoadhesion was introduced in controlled drug delivery system. Mucoadhesive is referred as ability of material to adhere to the mucous membrane. They are come together for prolonged period of time because of interfacial forces. Mucus secreted through goblet cell on the mucosal layer and is a viscoelastic fluid.

Bioadhesion can be divided into three types-

1. Type 1-Adhesion of two biological phases. e.g. platelets aggregation and wound healing.
2. Type 2-Adhesion of biological phase to substrate. e.g. cell adhere to culture.
3. Type 3-Adhesion of artificial material to biological phases. e.g. tooth enamel sealant.

Mucoadhesion is not difficult comparing with bioadhesion. In bioadhesion, the polymer adheres to biological membrane, if the substrate is mucus membrane the term mucoadhesion used. Mucoadhesion theories finally concluded that mucoadhesive polymer have physio-chemical properties which is related to mucus substrate.

Mechanism of mucoadhesion[5,6]

Mucoadhesion phenomenon which involving wetting, adsorption and interpenetration of polymer chains. Mucoadhesion having following stages-

1. Contact stage- Intimate contact between a Bioadhesive and membrane.
2. Consolidation stage-penetration of Bioadhesive into mucous membrane.

Advantages[5,8]

1. Increase residence time of dosage form at site of absorption.
2. Increase drug bioavailability due to first pass metabolism avoidance.
3. Help to improve the patient compliance and ease of administration.
4. protect drug degradation in acidic environment.
5. More onset of action.
6. It shows targeting and localized action at specific site.
7. Prolong residence time of drug molecule.
8. Excellent accessibility

Disadvantages.[4,5,7]

1. Drug cannot be administered by oral route because which irritate oral mucosa, have a better taste and odor.
2. Only small dose can be administered.
3. Vaginal formulation may interfere with sexual intercourse.
4. Vaginal formulation avoided during pregnancy.
5. It may get dislodged.
6. Formulation may cause the irritate the sensitive nasal mucosa.
7. The development of oral mucosal drug delivery system is the lack of model in vitro screening to identify drug.
8. Prolong drug contact possessing ulcerogenic property.

Theories of mucoadhesion[4,7,8]

Mucoadhesion involve following theories as follows –

1) Electronic theory

In electronic theory both mucoadhesive and biological materials possess opposing electrical charges. Attractive forces within the electronic double layer help to estimate mucoadhesive strength.

2) Adsorption theory

As per the adsorption theory the mucoadhesive adhere to mucus membrane by chemical interaction. such that, van der Waals and hydrogen bonds, electrostatic attraction or hydrophobic interaction. Hydrogen bonds are prevalent interfacial forces in polymer containing carboxyl group.

3) Wetting theory

This theory applied to liquids which prevent affinity to surface to spread on it. The contact angle which help to measure affinity. In generally rule state that lower the contact angle higher the affinity. For adequate spreadability contact angle may be zero.

4) Diffusion theory

Diffusion theory stated the interpenetration of polymer and mucous polymer chain is supported by diffusion theory. The bond strength increases with increases the degree of penetration. The penetration depends on conc. gradients and diffusion coefficients. Interpenetration found in the range of 0.2 to 0.5µm which helpful to form an effective bond strength.

5) Fracture theory

It includes the study of mechanical measurement of mucoadhesion. It identifies the force to separate two surfaces after adhesion. This force S_m is calculated in tests of resistance to rupture by the ratio of maximum

detachment force F_m and total surface area A_o, involved in adhesive interaction,

$$S_m = F_m/A_o$$

Since fracture theory depends on force required to separate the parts it does not consider the interpenetration.

6) Mechanical theory

Mechanical theory includes adhesion due to filling of the irregularities on a rough surface by mucoadhesive liquid. The roughness improves the interfacial area available to interaction.

Factor affecting the mucoadhesive drug delivery system[5,7,9]

Mucoadhesive of a drug carrier system to the mucous membrane depends on following factor-

Polymer based factor

1. Molecular weight of polymers, flexibility of polymer chains, spatial conformation, hydrogen bonding capacity, cross linking density, charge and concentration of polymers, degree of ionization.
2. Swelling or hydration factor of polymer.

2) Physical factor

P^H at polymer substrate, interface applied strength, contact time, moistening, presence of metal ion.

3) Physiological factor

Mucin turnover rate, disease state, renewal rate of mucosal cells, concomitant diseases, tissue movement.

Mucoadhesive Polymers[4,6,7]

These are water soluble as well as water insoluble polymers which are swellable in nature joined to each other by cross linkers. Mucoadhesive polymer divided into two classes as hydrophilic polymer and hydrogels. In which,

1) Hydrophilic Polymer - contains the carboxylic group exhibit mucoadhesive properties,

1. Polyvinyl Pyrrolidone (PVP)
2. Methyl Cellulose (MC)
3. Sodium Carboxy Methylcellulose (SCMC)
4. Hydropropyl Cellulose (HPC)
5. Other Cellulose Derivatives

2) Hydrogel - Swelling done when it absorbing water and adhere to the mucus layer. They are divided per their charge.

1. Anionic polymers- Carbopol, polyacrylates
2. Cationic polymer- Chitosan and its derivatives
3. Neutral / Non-ionic polymers- Eudragit (NE30D) analogues

Ideal characteristics of an mucoadhesive polymers[5,6,9]

1. They should not toxic and not easily absorbed from GI tract.
2. They should be non-irritant.
3. It should allow easy incorporation.
4. The polymer having less cost.
5. Polymer does not decompose on storage.
6. It have flexibility to penetrate the mucus membrane.
7. High molecular weight.
8. It should form a strong non – covalent bond with mucin-epithelial cell surface.
9. It allow incorporation to the drug and offer no hindrance to its release.

Recent generation of mucoadhesive polymer. [10,11]

Mucoadhesive directly adhere to cell surface. e.g. insertion of L-cysteine into thiolated polymers and target specific lecithin mediated adhesive polymer i.e.

1. Copolymers/ Interpolymer complex
2. Thiolated polymers(Thiomers)
3. Lectins

Mucoadhesive dosage forms[4,7]

The main aim of mucoadhesive dosage form are to provide intimate contact of the dosage form with absorbing surface to prolonged drug response. Because of mucoadhesion, certain water soluble polymers become adhesive on hydration. So, it increases extended period of drug molecule. In GI tract, the urogenital tract, the air ways, the nose, ear and eye there are mucosa line found. They include,

1. Gastrointestinal delivery system
2. Nasal delivery system
3. Ocular delivery system
4. Buccal delivery system
5. Vaginal delivery system
6. Rectal delivery system

Bioadhesive dosage forms[7,8,9,11]

Bioadhesive dosage forms can be developed as sublingual, buccal or gingival system for localized drug delivery at any site.

1. Buccal dosage forms-
   i. Adhesive tablets
   ii. Adhesive gels
   iii. Adhesive patches
   iv. Adhesive ointments

2) Sublingual

3) Dental or gingival

Evaluation parameter of mucoadhesive drug delivery system[4,7]

1) In vitro/ ex vivo tests

1. Determination of tensile strength
2. Determination of shear stress
3. In vitro drug release studies
4. Swelling method
5. Thumb method

6. Adhesion number
7. Electrical conductance
8. Viscometer method
9. Falling liquid film method
10. Flow channel method

2) In vivo method

1. Use radioisotopes
2. Use gamma scintigraphy
3. Use electron paramagnetic resonance oximetry
4. X-ray studies
5. Isolated loop technique

Recent generation:[4,7]

1. Bioadhesive Nano polymers as drug carriers
2. Alginate –polyethylene glycol-acrylate (alginate - PEGAC)
3. Poloxamers
4. Pluronics and combination
5. Other novel mucoadhesive polymers
6. Bacterial adhesions
7. Amino acid sequences
8. Antibodies

Recent mucoadhesion test:[5]

Currently mucoadhesion studies have been reported by using BIACORE integrated chip (IC) systems. These methods involve immobilization of the polymer on the surface of IC with subsequent passage of mucin solution over the same. Mucin –polymer interaction can be measured by an optical phenomenon called as surface plasma resonance(SPR), which measure change in the refractive index when mucin adhere on the polymer surface.

CONCLUSION

The mucoadhesive is approach of novel controlled drug delivery. The advantages of oral mucoadhesive drug delivery system which prolonged the residence time of drug which increases absorption of drug are important factor in oral bioavailability of many drugs.[5,7] In vivo and In vitro technique has been developed for mucoadhesive drug delivery system.[3] Improvement in mucoadhesive based oral delivery and in development of novel which is highly effective and mucosa compatible polymers which forms a clinical opportunity. The formulation of mucoadhesive drug delivery system depends on polymer with excellent mucosal adhesive properties and biocompatibility.[5,8] Hence, these novel mucoadhesive formulation require more work to delivered for both topical and systemic diseases treatment.[7]

REFERENCES

1. Recent advances in mucoadhesive buccal drug delivery systems and its marketed scope and opportunities by K.P. Sampath kumar, Debejit Bhowmilk, Amitsankar Dutta, Shravanpaswan, Lokesh Deb.
2. Theories and factors affecting mucoadhesive drug delivery systems: A review by Alexander Amit, Sharma Sharad, Ajazuddin, Khan Mohammed Junaid, Swarna.
3. Methods used to develop mucoadhesive drug delivery systems: Bioadhesion in the gastrointestinal tract by Fiebrig and S.S. Davis and S.E. Harding.
4. Novel mucoadhesive polymers- A Review by Mythri.G, K. Kavitha, M. Rupesh Kumar, Sd. Jagadeesh Singh.
5. Mucoadhesive drug delivery: Mechanism and methods of evaluation by Pranshu Tangri, Shaffi Khurana and N.V. Satheesh Madhav.
6. Critical review on mucoadhesive drug delivery systems by Vinod K.R, Rohit ReddyT, Sandhyas, David Banji, Venkatram Reddy B.
7. Recent advances in mucoadhesive /Bioadhesive drug delivery system: A Review by Phanindra B, B Krishna Moorthy and M Muthukumaran.
8. Mucoadhesive drug delivery system: An overview by Bindu M. Boddupali, Zulkar N.K. Mohammed, Ravinder Nath A, David Banji.
9. Mucoadhesive drug delivery system by Rahamatullah Shaikh, Thakur Raghu Raj Singh, Martin James Garland, A. David Woolfson, Ryan F. Donnelly.
10. Review on mucoadhesive drug delivery system: Novel approaches in modern era by Arshad Bashir Khan, Rajat Mohamana, Emlll Pal.
11. Mucoadhesive drug delivery system by Flavia Chiva Carvalho, Marcos Luciana Bruschi, Raul Cesar Evangelista, Maria Palmira Daflon Gremiao.