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MUCOADHESIVE DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

Mucoadhesion is an important consideration in the development of drug delivery systems. The Gastrointestinal Mucoadhesive drug delivery device increases and/or strengthens therapeutic effectiveness by extending the dosage form's residence time at the absorption site and enhancing personal interaction with the intestinal absorption surface. The mucoadhesion approach employing a polymeric drug delivery base includes, among other elements, wetting, adsorption, and interpenetration of polymer chains. Respective variables impact gastrointestinal retention and mucoadhesion.

KEYWORDS: mucoadhesive, theory, mucoadhesive dosage forms.

INTRODUCTION[1-4]

Oral administration is the most easy and recommended method of drug administration to the circulatory system. In the pharmacy sector, oral controlled release drug delivery has suddenly achieved interest as a way of delivering better therapeutic advantages such as convenience of dosage administration, patient compliance, and formulation variety. Drugs having short ½ and fast uptake from the gastrointestinal system exit the systemic circulation fast. These drugs should be dosed mostly to achieve adequate beneficial benefit. Oral sustained-controlled-release formulations are also being developed that resolve this limitation by slowly releasing the medication into the digestive tract and maintaining an appropriate drug concentration in the systemic circulation for an extended period. During topical application, such a dosage form will remain in the abdomen and release the drug in a controlled way, allowing the medicine to be administered continually to its site of absorption in the gastrointestinal system. Gastroretentive drug delivery systems could keep in the gastrointestinal area for a longer length of time, vastly improving medication gastric retention

time. Many gastroretentive drug delivery systems, including high density (sinking) devices retained in the stomach's base, have now been invented and developed during the previous few decades. Digestive fluids floating is caused by low density structures. extensible, flexible, or insoluble systems that control dose type emptying through the pyloric sphincter of the stomach, mucoadhesive systems that deliver adhesion properties to the mucosa of the stomach, expandable, expandable, or swellable systems that induce bioadhesion to the mucosa of the stomach Polymeric colloid systems magnetic systems, etc.

Mucus Membranes[5]

Mucosal barriers (mucosae) were its moisture surfaces that cover the walls of many internal cavities, like the gastrointestinal systems. A collagen layer (the membrane situ) and an epidermal cell with a saturated surface owing to the combination of a mucus layer make up the respiratory tract. Single-layered epithelia (such as gastrointestinal, small, and large intestines, and bronchi) or multilayered/stratified epithelia (such as stomach, small and large intestines, and bronchi) are both prevalent (e.g.in the esophagus, vagina, and cornea) Inside this first, goblet cells release mucus immediately onto vascular endothelium; in the latter, procedural such like digestive tract release mucus directly onto epithelial surfaces. Mucus exists in two forms: a gel layer that adheres to the mucosal surface and a lumen soluble or dispersed form. Mucous lipoproteins, lipids, inorganic salts, or water are the primary components among all mucosal hydrogel, with the latter accounting for more than 95% of total weight, resulting in a highly hydrated system. Mucus serves two basic purposes: protection and lubricating.

Mechanisms of Mucoadhesion[6]

Mucoadhesion has a few different mechanisms.

in two stages

1. Stage of contact
2. Stage of consolidation

The very first step is marked by interface between both the mucoadhesive and the mucosa, with the formulation spread and expanding and establishing deep interaction with mucous membrane. The delivery mechanism is physically attached in other situations, such as retinal or rectal formulations, while in others, such as for the nasal route, deposition is aided by the organ's aerodynamics. This amount of moisture activates the bioadhesive components during the consolidation process. Moisture softens the system, causing mucoadhesive particles to

separate and form weak intermolecular forces and hydroxyl groups. In general, there are two ideas that describe the consolidation process:

1. Diffusion theory is a theory that describes how information spread
2. The hypothesis of dehydration.

Both hydrogel polymers and mucous polypeptides interact by interdependence of their chain as well as the formation of new bonds, as according to diffusion of innovations. The bio adhesive device contains characteristics that favor combined chemical and physical interactions for this to happen.

MUCOADHESION CONCEPTS[7]

Here are several six main adhesive concepts that have been adopted for the study of bio adhesive:

According to the electrical theory: electrons Caused by the interaction of adherent areas transmission occurs. because of changes in their electrical structure This is it. planned to lead to the development of an electrical network a dual layer at the surface, followed by Intermolecular forces cause adhesion.

According to wetting theory includes surface or interfacial energy but is largely applicable to organic liquids. It refers to a liquid's capacity to spread rapidly over a surface, which is required for adhesive to form. An affection of a fluid for just a surface may be determined using methods including such interfacial tension goniometry, which measures the liquid's surface tension with both the substrate, the with basic rule would be that smaller the transition zone, the stronger the liquid's attraction for the solid.

According to adsorption theories explain when adhesives adhere together using hydrophobic interactions Waals's interactions. Those pressures are found to be the major factors to the sticky interaction. The chemisorption's hypothesis, for example, proposes that significant hydrogen bonds cause a contact across the surface.

According to the diffusion theory Increase the tendency of polymerization throughout a way to bond is described. Concentrations control the mechanism, which is influenced by the durations and density of accessible molecule chains. Its thermal conductivity and indeed the period of touch measure the direction of interdependence. A semi-permanent adhesives compound is broken when the surface area is adequate.

According to the mechanical principle, adherence is caused by a liquid adhesive engaging with imperfections on a large surface area after it has dried. Different materials, on either hand, give more contact area for contact with better viscous and plasticity energy absorption during composite action, which are regarded to be more significant throughout the adhesive processes than like a physical impact.

According to the fracture theory This varies from either 5 since it connects strength properties to the energy necessary to separate two areas implicated during attachment.

FACTORS AFFECTING MUCOADHESION[8]

A. Factors relating to polymers

1. Molecular mass

Its mucoadhesive strength rises with polymeric particle size up to 10000, below which it has little impact.

2. Active polymer concentrations

Thus, larger the polymeric content, the greater overall mucoadhesion in drug formulations for tablets. There is an ideal polymer content that results in the optimal mucoadhesion.

3. Polymer group flexibility

Interpretation and expansion need a high degree of flexibility.

B. Factors relating to the environment.

1. pH This charge upon on membrane of mucous and polymeric is affected by ph.

2. Applied strength It is important to provide a specific strength to establish a strong bio adhesive system.

3. Initial contact time as the original reaction temperature rises, so does the hydrogel strength.

4. Swelling depends on both polymers' concentration and on presence of water.

C. Factors on Physiology

1. Mucin reverse

a. Mucous renewal is predicted to reduce the mucoadhesive's resident duration on the mucous walls.

2. State of illness

b. Mucin renewal produces many soluble mucin molecules. Mucus has been shown to modify its chemical composition in sick states such as flu virus, liver damage, rheumatoid arthritis, muscular dystrophy, fungal diseases of the human body, as autoimmune reactions of retina.

POLYMERIC MATERIALS MUCOADHESIVE[8]

Mucoadhesive processes depend on even a product's or carrier's attachment to the mucosal surface. The proper carriers are necessary to facilitate this adhesion.

Mucoadhesive Polymers Ideal Characterization

Any polymers and bio adhesion promoting solution are added towards the preparation to aid in the adherence of the active medicinal component here to oral cavity. If in contact with body fluids, the agent might have extra qualities including enlargement help enhance breakdown.

1) Polymer should have a particle size of at least 100,00. This is required to increase the stickiness of the polymeric to the mucous.

2) Long chain polymers—the side chains should have been lengthy enough even to encourage interfacial adhesion but not so prolonged that diffusing becomes an issue.

3) It has a higher solubility.

4) String mobility and resistant of disintegration are measured by the extent of crossing bonding. Within case of moisture, highly long chain polymers expand and keep their shape. Swelling promotes regulated release profile and enhances polypropylene interfacial adhesion.

5) Official confirmation of space.

6) Polymeric chains flexibility—this facilitates polymer interfacial adhesion inside the mucous layer.

7) Polymer concentration—to improve mucoadhesive force, the polymeric must be at its optimal concentration. It is, though, dependent on the dose type.

8) Charged and intensity of ionization- Bernkop-Schnurch but also Freudl analysed the impact of polymeric energy on mucoadhesion. As concentration increased, ionized chitosan HCl demonstrated significant adhesiveness. The addition of such a non - ionic element to EDTA greatly enhanced mucoadhesive potency. For its small rate, the DTPA/chitosan combination had a lesser mucoadhesive efficacy than charged chitosan or hydrophobic EDTA chitosan combinations. As both a result, the order of mucoadhesive intensity is quinone.

9) Optimal staying hydrated hydration causes the production of a sliding gelatin, which reduces mucoadhesive strength.

10) Optimal pH – Mucoadhesion is greatest as high concentration, however at higher pH, its configuration changes into rod-like shape, allowing the mucoadhesion extra accessible for inter dispersion and interpretation. Positive charge polysaccharides such myosin generates polymeric compounds without mucous often at high pH conditions, resulting in major mucoadhesive forces.

11) It must be non-toxic, cost-effective, adaptable, and, ideally, disposable.

The following are some of the most common mucoadhesive polymers

Synthetic polymers

Polyvinyl alcohol, Polyamides

Polycarbonates, polyalkylene glycols

Polyvinyl ethers,

Esters and halides,

Polymethacrylic acid, polymethyl methacrylic acid,

Methylcellulose, ethyl cellulose, hydroxypropyl cellulose,

Hydroxypropyl methylcellulose,

Sod. Carboxymethylcellulose

Natural polymers

Pectin

Gelatin

Chitosan

Soluble starch

Sodium alginate

Guar gum

Xanthan gun

Tragacanth

Mucoadhesive Drug Delivery System Sites[9-13]

This **buccal cavity** does have a smaller capacity of about 50 cm2, yet it is a popular place for introducing effective drugs due to its ease of access. As order to treat the mouth diseases locally, its location allows for systemic delivery or pharmacologically active medicines by bypassing hepatic 1st metabolism.

nasal cavity

Its esophagus, just like buccal cavity, offers a prospective location and for design of compositions in which similarity transformation could play a vital role. This mucous membrane including its nose does have diameter of 150–200 cm^2. Inside this influx of human fine particles, average resident period of just a fine particle as in respiratory tract ranges among 15 to 30 minutes, that is related to enhanced mucous membrane action.

Eye conjunctiva

Because of all the high operation of weeping with blink of both the eyelids, the active medication is quickly evacuated from of the optical region, coupled with limited availability of that same active substances. The danger can be minimized by administering medicines through ophthalmic inlays or implanted.

GIT

Its Gastrointestinal have always considered a possible location for the introduction of mucoadhesive-based compositions. Investigators from around the global economy are interested and use bio adhesive polymeric to regulate the movement duration of delivery methods in a particular region of the intestinal tract. Similarity transformation such as chitosan, poly (acrylic acid), alginate, poly (methacrylic acid), and sodium carboxymethyl cellulose were utilized in the design of oral targeted delivery.

Dosage Forms[14-18]

Tablets

Tablets are tiny, round, and oval - shaped, with a size of 5–8 mm. Unlike traditional pills, mucoadhesive slater users to drink and talk while feeling nauseous. These dissolves, cling to the mucosa, and remain in place until full breakdown and/or release. Mucoadhesive tablets get the capability being used for sustained release drug discovery throughout particular but pairing chemical stability to a tablet will have extra advantages, such as integrated simulation and good biocompatibility of the drugs attributable to such a porous structure or a more elements found also with mucous membrane. Bio adhesive tablets may be customized to attach to any mucus layer, including those present in the abdomen, allowing for both localized and systemic controlled medication release.

Films

On flexibility and convenience, mucoadhesive films might well be preferable to adhesion tablets. They could also get around the oral gels' brief residence period just on mucosal, which is readily swept away and eliminated via saliva. Furthermore, in the event of local administration for oral illnesses, the films assist preserve the wound surface, reducing discomfort and allowing for more effective treatment. The ideal film would be flexible, stretchy, and smooth, yet robust enough to survive breaking due to tongue moving pressure. So addition to somehow maintained inside this tongue for said necessary period of action, it also must have excellent mucoadhesive strength. Swelling of the film, if it develops, should be kept to a minimum to avoid pain.

Patches

Patches are made up of three layers: an impervious base membrane, a medication reservoir layer that releases the medication in a regulated way, or a mucoadhesive area allowing mucosa adhesion. Transdermal medication delivery methods are comparable to patches systems. Solvent molding and indirect grinding are 2 ways for making bonded patch. The intermediary page via which patches be pierced is created using the solvent casting, that involves casts the drug mixed polymer(s) solutions onto a backing layer strip and then letting the solvent(s) to evaporation. All formation elements are uniformly distributed combined and compacted to the top slab inside this direct grinding process, after which patches of predefined diameter are cut as well as punched in. An impenetrable backing layer can be used to regulate drug release directions, help prevent loss, & reduce device distortion and dissolution throughout the application time.

List of various Patent

Sr. no.	Patent no.	Type of formulation	Year
Patents on floating drug delivery system			
1.	US 569638	Buoyant controlled release powder formulation	1992
2.	US 518229	Self-retaining GIT delivery device	1993
3.	US 522704	Sustained-release bilayer buoyant dosage form	1993
4.	US 566876	Floating system for oral therapy	1997
5.	US 627197	Gastro-retentive controlled-release microspheres	2001
6.	US 827843	Programmatic buoyant	2012

		delivery technology	
7.	US 888669	GR extended-release composition of the therapeutic agent	2014
8.	US 931430	Floating GR dosage form	2016
9.	US 956179	Controlled release floating pharmaceutical compositions	2017
Patents on mucoadhesive or bio adhesive systems			
1.	US 547270	Pharmaceutical CR composition with bioadhesive properties	1995
2.	US 5900247	Mucoadhesive for CR of the active principle	1999
3.	US 6303147	Bioadhesive solid dosage form	2001
4.	US 6306789	Mucoadhesive granules of carbomer suitable for oral administration of drugs	2001
5.	US 8974825	A pharmaceutical composition for the GI drug delivery system	2015
Patents on swelling an expandable system			
1.	US 4767627	Gastric retaining drug delivery device for controlled delivery of drugs	1988
2.	US 5443843	GRDDS for controlled release of drug	1995
3.	US 5780057	Pharmaceutical tablet exhibiting high volume increase when gets in contact with gastric fluids	1998
4.	US 5972389	Gastro-retentive, an oral dosage form for CR of sparingly soluble drugs	1999
5.	US 6488962	Tablets shape to enhance gastric retention	2002
6.	US 6548083	Prolonged-release drug delivery device adapted for gastric retention	2003
7.	US 6635280	Dosage form extending the duration of drug release in the gastric region during fed mode	2003
8.	US 6723340	Optimal polymer mixtures for gastric retentive tablets	2004
9.	US 6776999	Expandable GR therapeutically system for prolonged gastric retention time	2004
10.	US 7976870	Gastro-retentive oral dosage form with restricted drug	2011

		release in lower GIT	
11.	US9393205	GR tablets	2016
12.	US9801816	GR dosage form extended release of acamprostate	2017
Patents on raft forming systems			
1.	US 0119994	Gastric raft composition	2001
2.	US 0063980	In situ gel formation of pectin	2002
Other patents related to GRDDS			
1.	US 6635281	The gastric retaining liquid dosage form	2003
2.	US 6797283	Gastric retaining dosage form having multiple layers	2004
3.	US 8586083	GRDDS comprising an extruding hydratable polymer	2013
4.	US 9119793	GR dosage form of doxycycline	2015
5.	US 20150366832	GR dosage form for carbidopa	2015
6.	US 20150231084	Osmotic floating tablets	2015
7.	US 20160338949	Stabilized GR tablets of pregabalin	2016

Some of the marketed products of GRDDS

Brand Name	Active Ingredient	Dosage Form	Manufacturd B
Valrelease	Diazepam	Capsule, extended release; oral	Roche Labortores
Madopar	Benserazide and L-dopa	Dispersible Tablets	Roche Laboratrie
Liquid Gaviscon	Alum. Hydroxide and MgCO3	Liquid	GlaxoSmithKlin Consumer Helthcare Holdings (US) LLC
Topalkan	Alum.-Mg antacid	Solid dosage form	Pierre Fabre Drug, Franc
Conviron	Ferrous Sulphate	Solid dosage form	Conviro
Cifran OD	Ciprofloxacin	Solid dosage form	Sun pharmaceutical industries ltd
Glumetza	Metformin	Solid dosage form	Salix Pharmaceutical
Coreg CR	Carvidilol Phosphate	Solid dosage form	Sun pharm industries
Inon Ace Tablets	Simethicone	Solid dosage form	Sato Pharmaceutical Co., Ltd. - Drugs.com

CONCLUSION

This review in mucoadhesive formulations could prove to be a valuable tool in the development of new controlled drug delivery methods. Mucoadhesive drug delivery get a variety of applications, such as the creation of new mucoadhesive, tool wear, bio adhesion processes, and permeation improvement. Because of the flood of novel drug particles because of drug development, mucoadhesive dosage form will become increasingly more important in ensuring those compounds.

REFERENCES

1. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery system. Expert Opin. Drug Deliv, 2006; 3(2): 217- 33.
2. Iannucelli V, Coppi G, Bernabei MT, Camerorni R. Air compertment multiple-unit system for prolonged gastric residence. Part-I. Formulation study. Int J Pharm, 1998; 174: 47-54.
3. Rouge N, Allemann E, Gex-Fabry M, et al. Comparative pharmacokinetic study of a floatingmultiple-unit capsule, a high density multipleunit capsule and an immediate-release tablet containing 25 mg atenolol. Pharm Acta. Helbetiae, 1998; 73: 81.
4. Klausner EA, Lavy E, Friedman M, Hoffman A. Expandable gastroretentive dosage forms. J.Cont. Release, 2003; 90: 143-62.
5. Smart JD. The basics and underlying mechanisms of mucoadhesion. Adv Drug Deliv Rev., 2005; 57: 1556-68.
6. Akhtar M.H., Gupta J., Mohuddin M., Faisal M.D. (2012), A comprehensive Review on Buccal Drug Delivery System, Int. J. Of Pharm. Res. and Dev., 3(11): 59-77.
7. Smart J.D. (2005), The basics and underlying mechanisms of mucoadhesion, Adv. Drug Deliv. Rev., 57: 1556-1568.
8. 8.Gandhi S., Pandya P., Umbarkar R., Tambawala T., Shah M. (2011), Mucoadhesive Drug Delivery System- An Unusual Maneuver for Site Specific Drug Delivery System, Int J of Pharm Sci., 2: 132-152.'
9. Semalty M, Semalty A, Kumar G. Formulation and characterization of mucoadhesive buccal films of glipizide. Indian J Pharm Sci., 2008; 70: 43-8.
10. Hornof M, Weyenberg W, Ludwig A, Bernkop SA. Mucoadhesive ocular insert based on thiolated poly (acrylic acid): Development and *in vivo* evaluation in humans. J Control Release, 2003; 89: 419-28.
11. Sultana Y, Aqil M, Ali A. Ocular inserts for controlled delivery of pefloxacin mesylate: Preparation and evaluation. Acta Pharm, 2005; 55: 305-14.
12. Wagh VD, Inamdar B, Samanta MK. Polymers used in ocular dosage form and drug delivery systems. Asian J Pharmaceutics, 2008; 2: 12-7.
13. Asane GS. Mucoadhesive gastro intestinal drug delivery system:An overview. Pharmainfo.net, 2007; 5: 1-5.
14. 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.

15. Remeth D, Sfurti S, Kailas M. *In-vitro* absorption studies of mucoadhesive tablets of acyclovir. Indian J Pharm Educ Res., 2010; 44: 183-8.
16. 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.
17. Biswajit B, Kevin G, Thimmasetty J. Formulation and evaluation of pimozide buccal mucoadhesive patches. Int J Pharm Sci Nanotechnol, 2010; 2: 32-41.
18. Wong CF, Yuen KH, Peh KK. Formulation and evaluation of controlled release Eudragit buccal patches. Int J Pharm, 1999; 178: 11-22.