ISSN : 2320 4850

BI MONTHLY

Asian Journal of Pharmaceutical Research And Development

(An International Peer Reviewed Journal of Pharmaceutical Research and Development)

AJPRD

Volume - 01 Issue - 06 NOV-DEC 2013

website: www.ajprd.com

editor@ajprd.com

Asian Journal of Pharmaceutical Research and Development
(An International Peer-Reviewed Journal of Pharmaceutical Research and Development)
www.ajprd.com
ISSN 2320-4850

Review Article

NOVEL APPROACHES FOR MUCOADHESIVE GEL – A REVIEW

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Received: 13 January 2014 ***Revised and Accepted: 19 February 2014***

Abstract

Mucoadhesion can be defined as a state in which two components, of which one is of biological origin, are held together for extended periods of time by the help of interfacial forces. Mucoadhesive drug delivery systems is one of the most important novel drug delivery systems with its various advantages and it has a lot of potential in formulating dosage forms for various diseases and has controlled release of drug delivery system. Drug actions can be improved by developing new drug delivery systems, such as the mucoadhesive drug delivery system. These systems remain in close contact with the absorption tissue, the mucous membrane and release the drug at the action site leading to increase the bioavailability of drug and both local and systemic effects. So, carrier technology offers a novel approach for drug delivery by coupling the drug to a carrier particle such as microsphere, nanoparticle, liposome, etc. which modulates the release and absorption characteristics of the drug. Hence, the discussion focus on physiology of mucus, mucoadhesive dosage forms, and novel methods for mucoadhesive gel such as microemulsion, liposomal, microspheres based gel and their evaluation techniques.

Key Words: - Mucoadhesive drug delivery system, liposome, niosome, microemulsion, controlled release.

INTRODUCTION

The mucoadhesive dosage forms might be a useful tool for the efficient design of novel mucoadhesive drug delivery systems because it provides an intimate contact between mucus membrane and dosage from which increase the residence time and so subsequently increases the bioavailability, so there is sustained or controlled release drug delivery. Development of microparticulate such as liposomes, microemulsion, microspheres, nanoparticles mucoadhesive drug delivery system, which is able to improve the bioavailability of poorly absorbed drugs by prolonging their residence time and hence, reduction in frequency of dose.

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MUCUS

Mucus (or mucous) is slippery secretion produced by, and covering, mucous membranes. Mucous membrane (mucosae) is the moist surfaces lining the walls of various body cavities such as gastrointestinal and respiratory tracts. They consist of a connective tissue layer (the lamina propria) above which is an epithelial layer, the surface of which is made moist usually by the presence of a mucus layer. Mucous membrane of human organism is relatively permeable and allows fast drug absorption. [1]

Mucus is viscous colloid containing antiseptic enzymes (such as lysozyme) immunoglobulin's, inorganic salts, proteins such as lactoferrin and glycoproteins known as mucins that are produced by goblet cells in the mucous membrane. Mucin is the most important glycoprotein of mucus and it's responsible for its structure. [2]

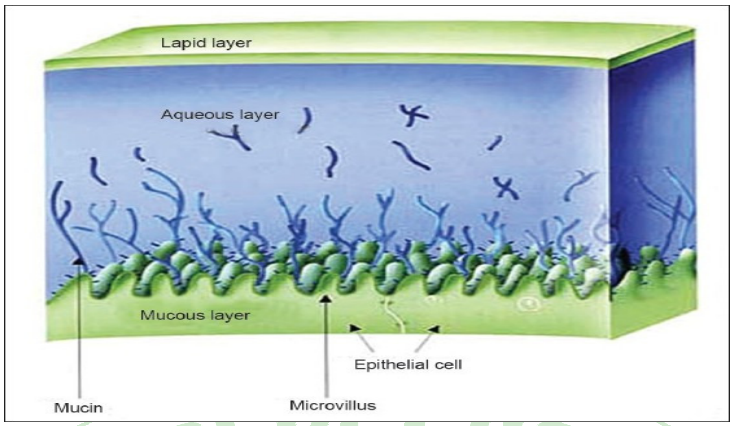


Figure 1 Structure of Mucus

Composition of Mucus Layer

- Water (95%)
- Glycoprotein and lipids (0.5-03%)
- Mineral salts (1%)
- Free protein (0.5-1%)

Functions of Mucus Layer

- **Protective**: to protect against infectious agents such as fungi bacteria and viruses.
- **Barrier**: The role of the mucus layer as a barrier in tissue absorption of the drugs and influence the bioavailability.
- **Adhesion**: mucus has strong adhesion properties.
- **Lubrication** : It is to keep the mucus membrane moist. Continous secretion from the goblet cell is necessary to compensate for the removal of the mucus layer due to digestion, bacterial degradation and solubilisation of mucin molecules[3]

Properties

- They are able to join together to make polymers or an extended three dimensional network i.e. gel.[2]

  The mucous site most used for drug administration and absorption is gastrointestinal but other routes also include nasal, oral, stomach, esophagus, intestinal etc

Some Examples of Mucosa

- **Oral Mucosa**

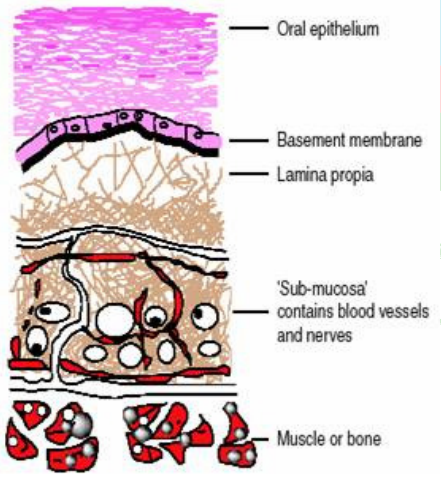


Figure 2: oral mucosa

- **Nasal Mucosa**

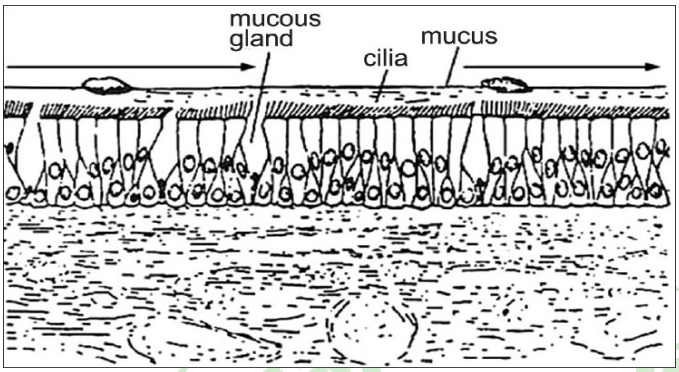


Figure 3: Nasal mucosa

- **Gastric Mucosa**

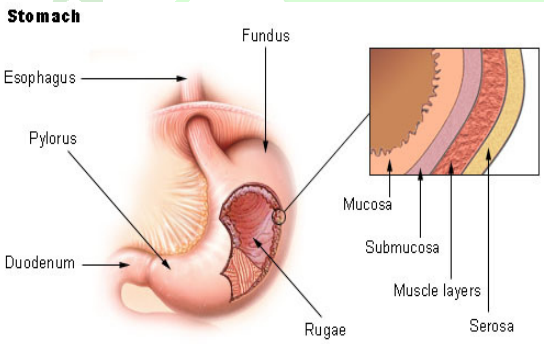


Figure 4: Gastric mucosa

- **Bronchial Mucosa**

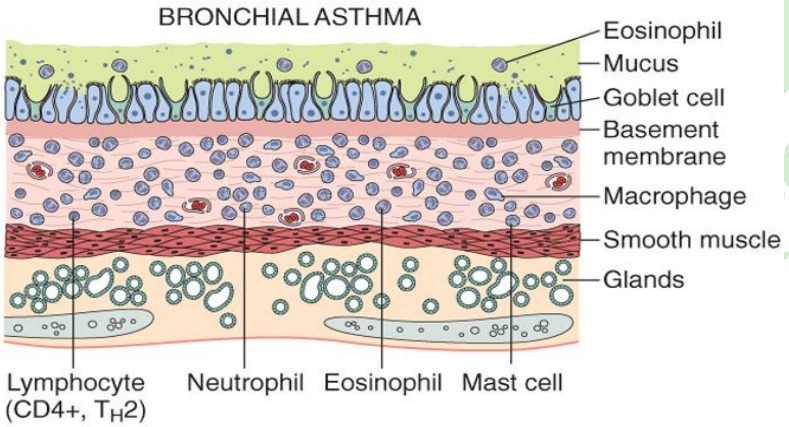


Figure 5: Bronchial Mucosa

MUCOADHESIVE DOSAGE FORMS

Definition

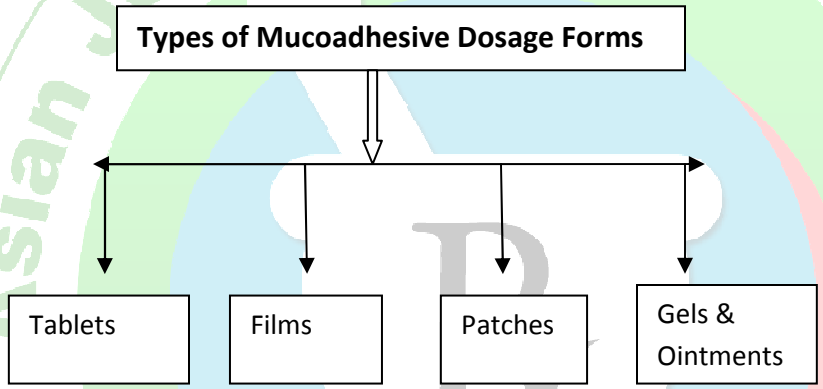
Mucoadhesive dosage forms may be designed to enable prolonged retention at the site of application, providing a controlled rate of drug release for improved therapeutic outcome. [1]

Need of Mucoadhesive Dosage Forms

Mucoadhesive dosage forms offer several advantages over other oral controlled release systems by virtue of prolongation of residence time of drug in gastrointestinal tract (GIT).

- Targeting and localization of the dosage form at a specific site.
- Also, the mucoadhesive systems are known to provide intimate contact between dosage form and the absorptive mucosa.[2]
- Application of dosage forms to mucosal surfaces may be of benefit to drug molecules not amenable to the oral route, such as those that undergo acid degradation or extensive first pass metabolism.[3]

Types of Mucoadhesive Dosage Forms



Tablets

Tablets are adhere to the mucosa, and retained in position until dissolution and/or release is complete. Mucoadhesive tablets offers efficient absorption and enhanced bioavailability of the drugs due to high surface to volume ratio and facilitates a much more intimate contact with the mucus layer. The application of mucoadhesive tablets to the mucosal tissues of gastric epithelium is used for administration offer localized action.

Mucoadhesive tablets are widely used because they release the drug for a prolonged period, reduce frequency of drug administration and improve the patient compliance. The drawback of mucoadhesive tablets is poor patient compliance because of unpleasant odor and taste. [1]

Films

Mucoadhesive films may be preferred over adhesive tablets in terms of flexibility and comfort. In addition, they avoid the relatively short residence time of oral gels on the mucosa, which are easily washed away and removed by saliva. Moreover, in the case of local delivery for oral diseases, the films also help protect the wound surface, thus helping to reduce pain, and treat the disease more effectively. An ideal film possesses good mucoadhesive strength in order to be retained in the mouth for the desired duration of action. [1]

Patches

Patches are laminates consisting of an impermeable backing layer, a drug containing reservoir layer from which the drug is released in controlled manner, and a mucoadhesive surface for mucosal attachment.

Patch system are those used in transdermal drug delivery. Two methods are used to prepare adhesive patches include solvent casting and direct milling. [1]

Gels and Ointment

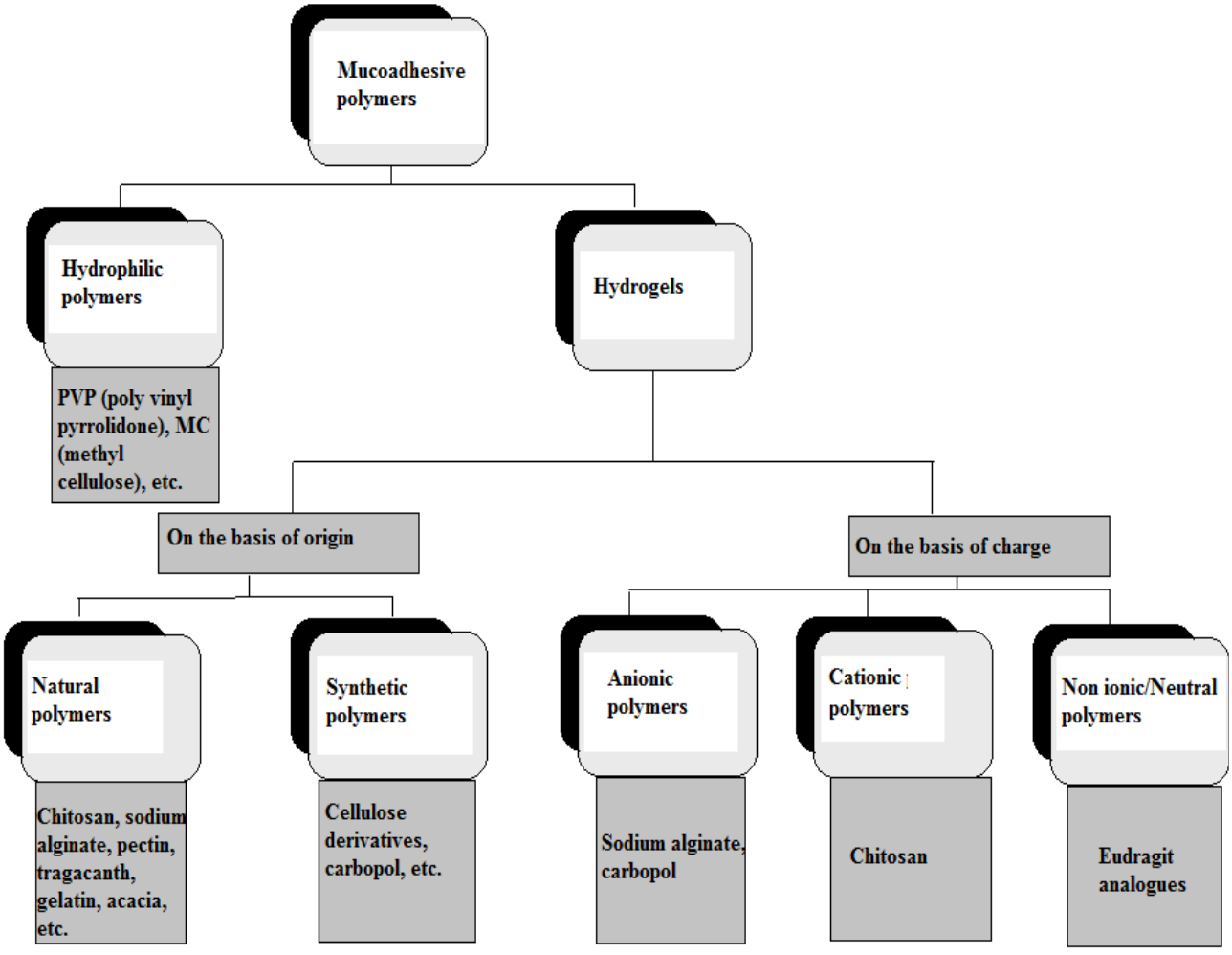
Semisolid dosage forms, such as gels and ointments, have the advantages of easy dispersion throughout the oral mucosa. However, drug dosing from solid dosage forms may not be as accurate as from tablets, patches or films. Poor retention of gels at the site of application has been overcome by using mucoadhesive formulations. Certain mucoadhesive polymers, for examples, sodium carboxymethycellulose, carbapol, 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. A major application of adhesive gels is the local delivery of medicinal agents for the treatment of periodontitis. [1]

MUCOADHESIVE POLYMERS [2]

Ideal Characteristics

- The polymer and its degradation products should be nontoxic.
- It should be non-irritant to the mucus membrane.
- The bioadhesive must spread over the substrate to initiate intimate contact and increase the surface area of contact.
- It should adhere quickly to mucosa.
- It should allow easy incorporation of the drug and must release the drug at the desired rate.
- The cost of the polymer should not be high.
- It should show bioadhesive properties in both dry and liquid state. [2]

Classification and examples of mucoadhesive polymers



Examples of Mucoadhesive Polymers
Carbapol

properties	**White, puffy, acidic, hygroscopic powder with a slight characteristic odor**
Molecular weight	1×10^6 - 4×10^6
Viscosity	400 cps at 25 ºC with 0.5% aqueous solution.
Density	$5g/cm^3$ in bulk, 1.4g/cm3 tapped
pH	2.5 – 3.0
Solubility	soluble in water , alcohol and glycerin.
Uses	Excellent thickening, emulsifying, suspending and gelling agent.

Chitosan ([1-4] 2- amino – desoxy – β – D – glucan)

preparation	**Prepared from chitin of crabs and lobsters by N-deacetylation with alkali.**
solubility	Soluble in dilute acids to produce a linear polyelectrolyte with a high positive charge density and forms salts with inorganic and organic acids
mucoadhesion	either secondary chemical bonds such as hydrogen bonds or ionic interactions between the positively charged amino groups of chitosan and the negatively charged sialic acid residues of mucins.

Hydroxypropylmethylcellulose (HPMC)

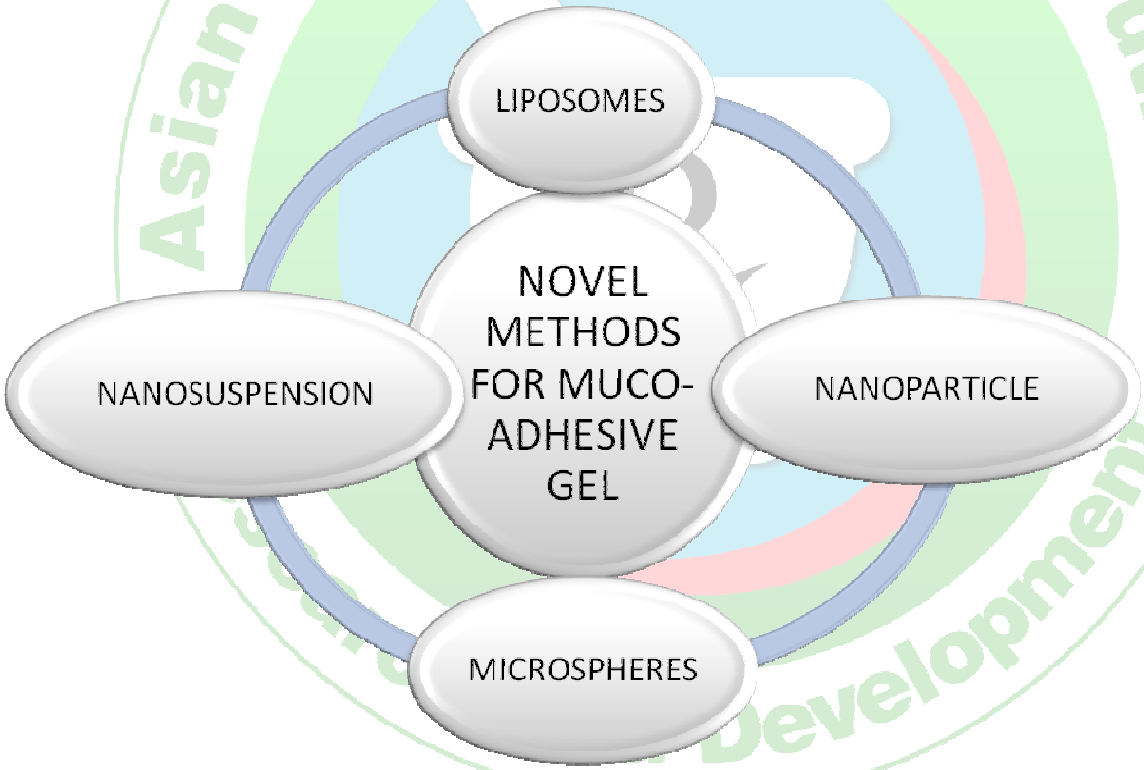
Description	**Odorless, tasteless, white or creamy white fibrous or granular powder**
Grades	Methocel E5, El 5, E50, E4M,F50, F4M, K100, K4M, K15M, K100M.
pH	3-11
Mw	8.6×10^4
Viscosity	El 5- 15cp , E4M – 400cp and K4M – 4000cp (2% aqueous solution)
Solubility	soluble in cold water, mixtures of mythelene chloride and isopropyl alcohol. It is insoluble in alcohol, chloroform, ether
Uses	suspending agent, viscosity builder, film forming agent, tablet binder and as an ingredient in adhesive ointment

Sodium Alginate

source	**The purified carbohydrate products extracted from brown seaweeds by the use of dilute alkali and occurs as a buff powder , which is odorless and tasteless.**
pH	7.5
viscosity	20-400cps (1% aqueous solution)
solubility	soluble in water , forming a viscous colloidal solution and is insoluble in other organic solvents and acids where pH of the resulting solution falls below 3.
uses	Paste and creams, emulsion stabilizer, suspending agent, tablet binder, tablet disintegrant.

APPROACHES FOR MUCOADHESIVE GELS

There are various approaches for formulation of mucoadhesive gel. Some are as follows:



Mucoadhesive Microemulsion Gel

Suryanarayan Mandal et al. developed Carbamazepine Mucoadhesive Microemusion for Intranasal Delivery, to enhance the aqueous solubility and to accomplished intranasal delivery of drug to brain. They prepared carbamazepine microemulsion by using Labrafil M 1944CS as an oil, Accenone CC as surfactant & Transcutol P as cosurfactant by titration method and Carbapol 934 used as mucoadhesive polymer.

In the result, they found that the mucoadhesive microemulsion are stable and can target the drug to brain through intranasal route and thus can play an alternative for conventional dosage form. [5]

Ashwini Rasal, HS Mahajan developed nasal mucoadhesive microemulsion of sumatriptan succinate, to enhance the brain uptake of the drug

in o/w microemulsion which was suitable for intranasal delivery. They prepared microemulsion system containing tween 80, span 80 as surfactant & n-butanol as a cosolvent & isopropyl myristate as oil. HPMCk15M used as mucoadhesive polymer The result demonstrated that the sumatriptan succinate was found to be fairly rapid, as it converts into gel inside the nasal cavity and increase the residence time & could improve bioavailability of the drug.[6]

K.Jaya Raja Kumar, Selvadurai Muralidharan evaluated anti-fungal activity of microemulsion fluconazole gel for Onychomychosis against Aspergillus Niger. They have done this study to evaluate microemulsion for topical drug delivery and to expand microemulsion based gel of fluconazole for the treatment of onchomychosis. They prepared formulation using oleic acid as an oil, mixture of surfactant (tween 80), cosurfactant (propylene glycol) and water. The result obtained that the optimized gel showed better penetration & mucoadhesive properties as compared to commercial gel.[7]

Mucoadhesive Liposomal Gel

Ibrahim A. alsarra & Amel Y. Hamed developed Acyclovir liposomes for intranasal systemic delivery; they used liposomes as a biocompatible carrier to improve delivery properties across nasal mucosa. They have studied this to formulate acyclovir liposome and partition into Poly –N-vinyl-2-pyrrolidone. They prepared formulation contain carbapol, chitosan, and Poly –N-vinyl-2-pyrrolidone were used in acyclovir liposome by conventional thin-film hydration method. Finally, the result found that the use of acyclovir liposome & mucoadhesive gel not only promoted the prolonged contact between the drug and the absorptive sites in the nasal cavity, but also facilitated direct absorption through the nasal mucosa.[8]

Ghada Abdelbery developed ocular Ciprofloxacin hydrochloride mucoadhesive Chitosan-coated liposome; to improve the ocular bioavailability of ciprofloxacin hydrochloride through the preparation of ocular mucoadhesive chitosan coated liposomes. They prepared liposome by the thin film hydration technique, using different molar ratios of L-α-phosphatidyl choline, cholesterol, stearylamine and diacetyl phosphate. They have concluded that the chitosan coated liposome could be a promising approach to increase the ocular bioavailability of ciprofloxacin. [9]

Mohammed M. Mehana, Hoda A. Elmarandy and Magda W. Samaha, assessed physically and microbiologically, the mucoadhesive liposome as ocular delivery system, to improve the ocular permeation of drug and enhanced antimicrobial activity. They prepared ciprofloxacin HCl-loaded reverse phase evaporation liposomes were coated with different concentration and molecular weight of mucoadhesive biocompatible chitosan polymer to form chitosomes. In the result, they obtained that liposome coating process resulted in entrapment efficiency reduction and higher chitosan concentration. Chitosan coating improved the ocular permeation of ciprofloxacin- HCl .This formulated system enhanced antimicrobial activity of ciprofloxacin HCl against both gram positive and gram negative bacteria. [10]

Mucoadhesive Microsperes Gel

Canan Hascicek, Nursin Gonul designed mucoadhesive microspheres containing Gentamicin Sulphate for nasal administration in order to provide the absorption of a highly polar drug through nasal mucosa. They prepared formulation containing Hydroxypropyl methyl cellulose as a mucoadhesive polymer, sodium cholate by spray drying technique.The result obtained that the formulation increased residence time of the microspheres on the mucosa and increased the absorption of drug through nasal mucosa. [11]

Nazia khanam, Anupam sachan, designed mucoadhesive microspheres of novel NSAID drug using algino-eudragit RS100 system by using combination of algino-eudragit RS100 system by ionic gelation technique. The result found that formulations showed improved flow behavior as compared to pure drug. [12]

Mucoadhesive Nanoparticle Gel

Yousefpour P., Atyabi F. prepared and compared of Chitosan nanoparticle with different degrees of glutathione thiolation; they used chitosan as biocompatible carrier to improve delivery of active agent by applying this vehicle in the form of nanoparticle to increase efficacy of active agents. They depolarized chitosan by using sodium nitrite method and prepared nanoparticles by ionic gelation method.

They have concluded from the result, thiolation improves the stability of chitosan without any changes in size and charge of nanoparticles, but affects the nanogel structure. [13]

Mohammed s. khan, Rohitash k developed nasal mucoadhesive nanoparticles of an analgesic drug;

They prepared mucoadhesive nanoparticles of chitosan using tramadol hydrochloride by spray drying method by using drug to polymer ratio.

They concluded from the result that the Tramadol HCl loaded chitosan nanoparticles is promising delivery through nasal route which successfully relieved pain causing no damage to nasal mucosa. [14]

Mucoadhesive Nanosuspension Gel

Dhaval J Patel and Jayvadan K Patel designed a Famotidine loaded mucoadhesive nanosuspension for Aspirin induced ulcer treatment by using the media milling technique and allowing significant reduction in ulcer index compared to famotidine suspension. They have used the drug nanoparticles system treated with mucoadhesive polymers because these small particles have ability to penetrate in the mucus layer and bind to underlying epithelium and adhere directly to the mucus network. Thus, the particle uptake into the disrupted barrier in gastric ulcerations could allow the accumulation of the particulate carrier system in the desired area. Hence, subsequent increase in local drug concentration prolongs the residence time of the drug in the gut and, therefore, increases the time when absorption can occur. In the result, they found that mucoadhesive nanosuspension containing famotidine nanocrystals could produce added value by allowing a reduction in ulcer index compared to famotidine suspension. [15]

Mucoadhesive Niosomal Gel

Deepika Agrawal , Indu P. Kaur improved pharmacodynamic of timolol maleate from a mucoadhesive niosomal ophthalmic drug delivery system. They prepared Chitosan and Carbopol coated niosomal timolol maleate formulations by reverse phase evaporation and compared to timolol solution in terms of in vitro release and IOP lowering pharmacodynamic effect.

In this result, they found that the formulation indicated lesser systemic side effects by lowering IOP and reducing with REV. [16]

EVALUATION OF MUCOADHESIVE GEL

Tests measuring Mucoadhesive Strength

Mucoadhesive strength is the force required to break the binding between the model membrane and mucoadhesive.Depending on the direction in which the mucoadhesive is separated from the substrates, it is possible to obtain the detachment, shear, and rupture tensile strengths as indicated in figure 7. [17]

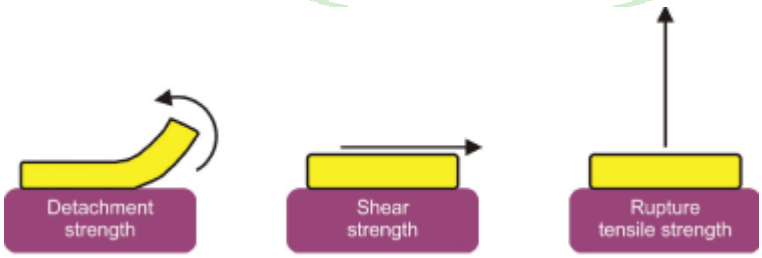


Figure 6: Different forces evaluated in mucoadhesion tests.

Determination of Tensile Strength

Method using the tensile strength measure the force required to break the adhesive bond between a model membrane and the test polymers. The equipment used to measure tensile strength is Texture Analyzer or a Universal testing machine.In this test, the force required to remove the formulation from a model membrane is measured, which can be a disc composed of mucin, a piece of animal mucous membrane, and generally porcine nasal mucous or intestinal mucus from rats. Based on results, a forced distance curve can be plotted which yields the force required to detach the mucin disc from the surface with the formulations, the tensile work (area under the curve) during the detachment process , the peak force and the deformation to failure. This method is more frequently used to analyze solid systems like microspheres, or semi solid material.In addition to rupture tensile strength, the texture analyzer can also evaluate the texture of the formulations and assess other mechanical properties of the system.

Figure 7: Bioadhesion test using the texture analyzer

A mobile arm containing a probe forces down into a sample held in a flask placed on the equipment's platform. Speed rate, time and depth are preset. From the resulting force-time and force- distance plots, it is possible to calculate hardness (force required to given deformation), compressibility (force required to deform the product during the compression), adhesiveness (work required to overcome the attraction forces between the surfaces of sample and probe). Using this technique, it is possible to perform previous evaluation of the materials adhesive capacity, evidencing mucoadhesive properties. [17]

Determination of Shear Strength

This test measure the force required to separate two parallel glass slides covered with the polymer and with a mucin film. This can also be done using, Wilhemy's Model.In which a glass plate is suspended by a microforced balance and immersed in a sample of mucus under controlled temperature. The force required to pull the plate out of sample is then measured under constant experimental conditions. Although measures taken by this method are reproducible, the technique involves no biological tissue and therefore does not provide a realistic stimulation of biological conditions.

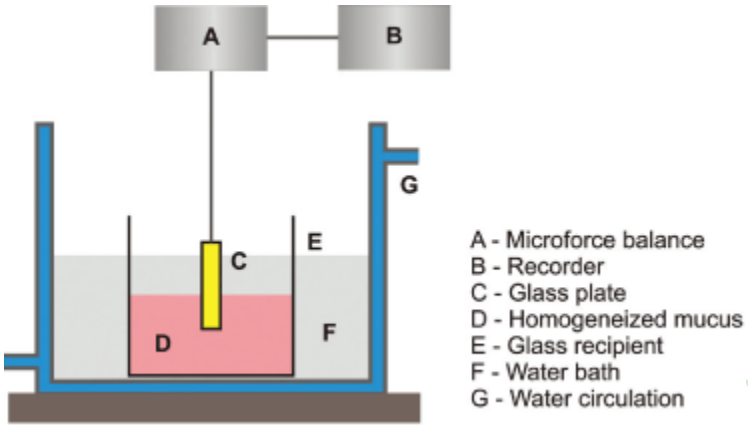


Figure 8: Apparatus to determine mucoadhesion in vitro, Using Wilhemy's technique

Wilhemy's plate technique or microforce balance technique can also be modified in order to measure the specific adhesion force of microparticles. This involves the use of microtensiometer and a microforce balance and is specific, yielding both contact angle and surface tension. The mucous membrane is placed in a small mobile with both pH and controlled physiological temperature. A microsphere attach through a thread to the stationary microbalance. The chamber with the mucous membrane is raised until it comes into contact with microsphere, and after contact time, is lowered back to the initial position. [17]

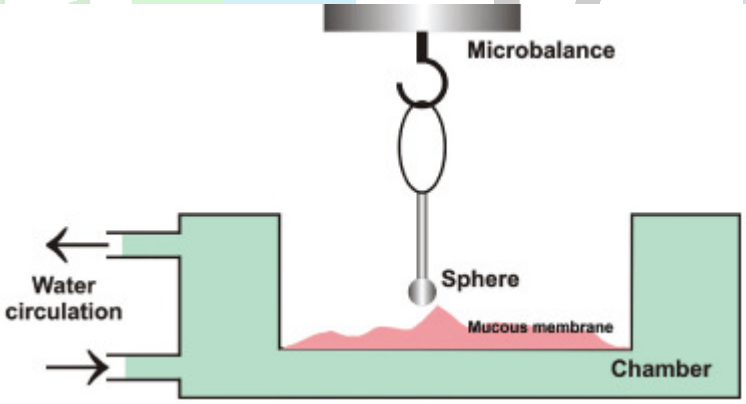


Figure 9: Microbalance Method for Measuring Mucoadhesion

Advantage of microforce balance

Simulating physiological condition and result obtained at more microscopic level, besides being more reproducible and sensitive.

Disadvantages of microforce balance

It is not indicated for microsphere smaller than 300 µm. [17]

Thumb test

The adhesiveness is measured by the difficulty of pulling the thumb from the adhesive as a function of the pressure and the contact time. Although thumb test may not be conclusive, it provides useful information on mucoadhesive potential of the polymer. It is important consideration for the development of buccal adhesive drug delivery systems. [2]

Falling Liquid Film Method

This is used to study the mucoadhesion. The chosen mucous membrane is placed in a stainless steel cylindrical tube, which has been longitudinally cut. This support is placed inclined in a cylindrical cell with a temperature controlled at 37 ºC. An isotonic solution is pumped through the mucous membrane and collected in a beaker. Subsequently, in the case of particulate system, the amount remaining on the mucous membrane can be counted with the aid of a coulter counter.

For semisolid, the non adhesive mucoadhesive can be quantified by performance liquid chromatography. In this later case, porcine stomach, intestine and buccal mucus were tested. This method showed that type of mucus used does not influence the result. [17]

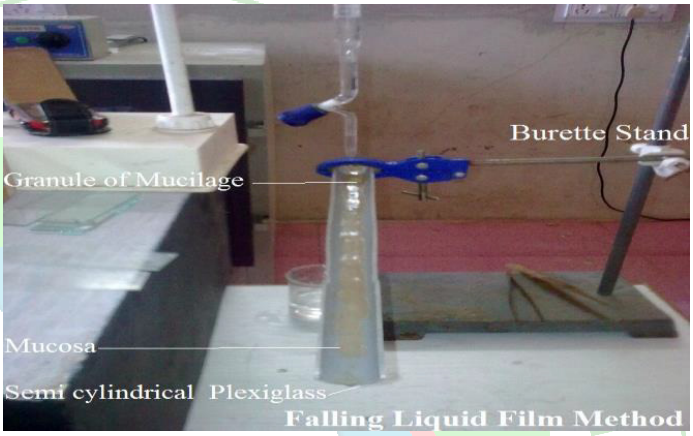


Figure 10 Falling Liquid Film Method

Particle size measurement

- Particle size analysis for microemulsion can be determined by photon correlation spectroscopy with a Beckman N5 submicron particle size counter which can measure the size range from 5nm to approximately 3µm. [6]
- Another instrument is dynamic light scattering method employing a particle sizer 1, 3, 5 by which the particle size of microemulsion should be less than 150 nm can be measured. [6]
- The particle size of liposomes can be measured by a laser particle analysis technique using Brookhaven Instruments.[8]
- The particle size of microspheres can be measured by optical microscopy.

In-vitro diffusion study

In-vitro diffusion study can be performed by Franz diffusion cell having specific diameter. Dialysis membrane having molecular weight cut off range 12000 – 14000 k Da used as diffusion membrane. Pieces of dialysis membrane should soak in phosphate buffer prior to experiment. Diffusion cell then filled with phosphate buffer and dialysis membrane then mounted on the cell. The temperature should maintain at 34^{o}C. After a pre-incubation time, the microemulsion drug placed in the donor chamber. Samples periodically withdrawn from the receptor compartment at particular intervals and replaced with the same amount of fresh phosphate buffer solution, and assayed by a spectrophotometer. [11]

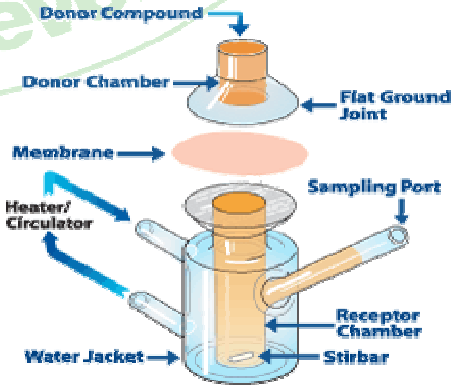


Figure 11: Franz diffusion cell

In-vitro permeation study

This study is performed same as diffusion study, only the difference is that the biological membrane should be use instead of dialysis membrane.

Determination of Viscosity:

Viscosity of the formulation can be measured by using Brookfield digital viscometer.[18]

Determination of Drug Content Uniformity:

Drug content uniformity can be determined by using appropriate analytical method UV spectrophotometer, HPLC etc.

Spreadability

In case of topical use the spreadability should indicate that the gel is easily spreadable by small amount of shear. A good gel takes less time to spread and will have high spreadability. [7]
Spreadability can be determined by an apparatus suggested by Muttimer et al., It consist of a wooden block which is provided by a pulley at one end. A rectangular ground glass plate is fixed on this block. An excess of formulation (about 3 gm) under study should be place on this ground plate. The formulation then sandwich between this plate and another glass plate having the dimensions of the fixed ground plate and provided with the hook. A 1 Kg. weight was placed on the top of the two plates for 5 minutes to expel air and to provide a uniform film of the formulation between the plates. Excess of formulation scrapped off from the edges. The top plate then subjected to a pull of 50 gms, with the help of a string attached to the hook and the time (in seconds) required by the top plate to cover a distance of 10 cm is noted. A shorter interval indicates better spreadability.
The spreadability can be calculated using the formula:
$S = m \times l / t$
Where S = Spreadability;
m = weight tied to the upper slid; l = length of the glass slid; t = time. [19]

Evaluation of in situ gel:

Determination of pH:

The PH of the gel can be determined by using a calibrated pH meter. [20]

Swelling studies:

Mucoadhesive dosage forms weigh individually (w1) and place separately in Petri dishes containing buffer at regular intervals. (5, 1, 2, 3,4,5,6 hours) the dosage forms remove from the Petri dishes and excess surface water remove using filter paper. Reweigh dosage form and swelling index (SI) can be calculated as follows,
$SI = (W2-W1)/W1$ [21]

Entrapment Efficiency

Entrapment efficiency can be calculated in case of liposome based approach by using the following equation:
Encapsulation efficiency = $(E0 - E1) / E0 \times 100$
Where, E0 = amount of drug added initially,
E1 = amount of drug determined, and
(E0-E1) represents the amount of drug trapped in the formulation. [8]

Table 1: Examples Of Gelling Agent Which Are Reported For Mucoadhesive Gel Formulation

Drug	*Category*	*Basic Formulation*	*Gelling Agent*	*Muco-Adhesive Strength*	*Muco – Adhesive Time*	*Release (Hours)*
Flourouracil	Anticancer	Transbuccal Gel	Poloxamer 407, HPMC	$12.8\pm1.4\times10^3$	8.08±1.85	8
Gatifloxacin	Antibacterial	Ophthalmic Gel	Sodium Alginate(23)	-----	12	12
Venlafaxine Hydrochloride	Ant anxiety	Mucoadhesive Nasal Gel	Carbopol 934, Sodium	19.25±0.55	-----	12
Bifonazole	Antifungal	Mucoadhesive In-situ Gel	Carbopol 934, Poloxamer	1872	-----	-----
Clotrimazole	Antifungal	In-situ Gel	HPMC, Carbopol 934	54±5.6	-----	6
Diclofenac Sodium	NSAID	Mucoadhesive Hydrogel	HPMC, Carbopol 934	48±0.6	5.5	6
Satranidazole	Antifungal	Mucoadhesive Hydrogel	Sodium CMC,	167.72±3.76	-----	8
Timolol Maleate	Glaucoma	Niosomal Ophthalmic gel	Carbopol 934P/ 947P,	-----	-----	10
Fluconazole	Antifungal	Microemulsion Gel	Carbopol (30)	-----	-----	-----
Clotrimazole	Antifungal	Microemulsion Gel	Carbopol Etd 2020 (31)	-----	48±3.5 min	12

FUTURE TRENDS

Researchers found that the fate of buccal adhesive drug delivery turning towards vaccine formulations and delivery of small proteins or peptides. According to polymer science, newer mucoadhesive polymers with the added attributes of being biodegradable, biocompatible, non-toxic, and which could also function as enzyme inhibitors for the successful delivery of proteins and peptides.

CONCLUSION

Microparticulate mucoadhesive system are particularly interesting because they offer protection to therapeutic entities as well as enhanced absorption that result from increased contact time provided by the mucoadhesive component. Microparticulate system and mucoadhesive drug delivery system through various approaches play fundamental role to improve the bioavailability of drug. Development of liposomal, microemulsion, microspheres, nanoparticle mucoadhesive drug delivery system, which is able to improve the bioavailability of poorly absorbed drugs by prolonging their residence time, through facilitating the intimate contact of the delivery system with the absorption membrane, reduction in frequency of dose, increased patient compliance.

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