

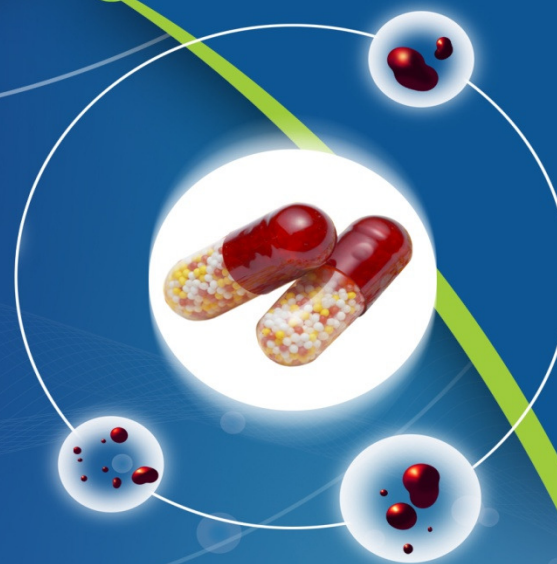


**BI  
MONTHLY**

**ISSN: 2320-4850**

# Asian Journal of Pharmaceutical Research And Development

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



**A  
J  
P  
R  
D**

**Volume - 01**

**Issue - 01**

**JAN-FEB 2013**

**website: [www.ajprd.com](http://www.ajprd.com)  
editor@ajprd.com**



---

**Review Article**

---

**A REVIEW ON MUCOADHESIVE TABLETS AS CONTROLLED DRUG DELIVERY SYSTEM****Megha Jain\*, Natasha Sharma, M.P.Khinchi, Dilip Agrawal,**Department of Pharmaceutics, Kota College of Pharmacy, **Kota (Raj.)****Received: 23 January 2013****Revised and Accepted: 15 February 2013****ABSTRACT**

*Stomach-specific mucoadhesive tablets as a controlled drug delivery system have been developed to increase gastric retention time of the dosage forms. This article presents the polymers use for mucoadhesive tablets, factor affecting the mucoadhesion, and developments in the techniques for in vitro and in vivo evaluation of mucoadhesive tablets have also been discussed.*

**Key words:** Evaluation, Gastric Retention Time, Mucoadhesive Tablets, Polymers

**INTRODUCTION**

Oral controlled release (CR) dosage forms (DFs) have been developed for the past three decades due to their considerable therapeutic advantages. [1] However, this approach has not been suitable for a variety of important drugs, characterized by a narrow absorption window in the upper part of the gastrointestinal tract, i.e. stomach and small intestine. This is due to the relatively short transit time of the DF in these anatomical segments. Thus, after only a short period of less than 6 h, the CR-DF has already left the upper gastrointestinal tract and the drug is released in nonabsorbing distal segments of the gastrointestinal tract.

This results in a short absorption phase that is often accompanied by lesser bioavailability. The medications that are included in the category of narrow absorption window drugs are mostly associated with improved absorption at the jejunum and ileum due to their enhanced absorption properties, e.g. large surface area, in comparison to the colon or because of the enhanced solubility of the drug in the stomach as opposed to more distal parts of the gastrointestinal tract. [2]

It was suggested that compounding narrow absorption window drugs in a unique pharmaceutical DF with gastro retentive properties would enable an extended absorption phase of these drugs. After oral administration, such a stomach-specific mucoadhesive tablets would be retained in the stomach and release the drug there in a controlled and prolonged manner,

---

\*Correspondence author  
Megha Jain  
Kota College of Pharmacy, Kota, Rajasthan

so that the drug could be supplied continuously to its absorption sites in the upper gastrointestinal tract. This mode of administration would best achieve the known pharmacokinetic and pharmacodynamic advantages of stomach-specific mucoadhesive tablets for these drugs. [3] Under certain circumstances prolonging the gastric retention of a delivery system is desirable for achieving greater therapeutic benefit of the drug substance. For example, drugs that are absorbed in the proximal part of the gastrointestinal tract and drugs that are less soluble in or are degraded by the alkaline pH may benefit from prolonged gastric retention. In addition, for local and sustained drug delivery to the stomach and proximal small intestine to treat certain conditions, prolonged gastric retention of the therapeutic moiety may offer numerous advantages including improved bioavailability and therapeutic efficacy, and possible reduction of dose size. It has been suggested that prolonged local availability of antibacterial agents may augment their effectiveness in treating *H. Pylori* related peptic ulcers. [4-6] 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, e.g. efficient absorption and enhanced bioavailability of the drugs due to a high surface to volume ratio, a much more intimate contact with the mucus layer. Mucoadhesive tablets can be tailored to adhere to any mucosal tissue including those found in stomach, thus offering the possibilities of localized as well as systemic controlled release of drugs. The application of

mucoadhesive tablets to the mucosal tissues of gastric epithelium is used for administration of drugs for localized action. Mucoadhesive tablets are widely used because they release the drug for prolong period, reduce frequency of drug administration and improve the patient compliance. [7]

Interest in controlled and sustained release drug delivery has increased considerably during the past decade and, in selected areas, it's now possible to employ fairly sophisticated system which is capable of excellent drug release control. The self-regulating insulin delivery system by using lectin and oral osmotic tablet are illustrative examples. However, for oral administration, all of these systems are limited to some extent because of gastrointestinal (GI) transit. Thus, the duration of most oral sustained release products is approximately 8-12 hours due to the relatively short GI transit time, and the possibilities to localize drug delivery system in selected regions of the gastrointestinal tract (GIT) for the purpose of localized drug delivery are under investigation. Several approaches have been suggested to increase GI transit time, addressing the issue of localized drug delivery. The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion, flotation, sedimentation, expansion, modified shape systems, or by the simultaneous administration of pharmacological agents that delay gastric emptying Both low and high-density drug delivery systems have been suggested as possible approaches to extend the transit time but the results of exploratory studies area equivocal. In another system in which particle size, relative to stomach retropulsion has

been suggested as a means to delay stomach emptying and thereby prolong transit time. This phenomenon is also relatively short duration, particularly drug delivery system administered in absence of food. An alternative approach is to employ mucoadhesive polymers that adhere to mucin/ epithelial surface. Such polymer applied to any mucus membranes and perhaps non-mucus membrane as well. Thus, mucoadhesive polymers would find application in the eye, nose, vagina and GIT including the buccal cavity and rectum. An ideal dosage form is one, which attains the desired therapeutic concentration of drug in plasma and maintains constant for entire duration of treatment. This is possible through administration of a conventional dosage form in a particular dose and at particular frequency. In most cases, the dosing intervals much shorter than the half life of the drug resulting in a number of limitations associated with such a conventional dosage form are as follows:

- Poor patient compliance; increased chances of missing the dose of a drug with short half-life for which frequent administration is necessary.
- A typical peak plasma concentration time profile is obtained which makes attainment of steady state condition difficult.
- The unavoidable fluctuation in the drug concentration may lead to under medication or over medication as the steady state concentration values fall or rise beyond in the therapeutic range.
- The fluctuating drug levels may lead to precipitation of adverse effects especially of

a drug with small therapeutic index whenever overmedication occurs.

The above problems can be over come by the development of effective and safer use of existing drugs through concepts and technique of controlled and targeted drug delivery system. The controlled drug delivery system is one, which delivers the drug at a predetermined rate, locally or systemically for a predetermined period of time. The targeted drug delivery system is one, which delivers the drug only to its site of action and not to the non target organs or tissues.

The advantages of controlled drug delivery system over the conventional dosage form are as follows;

- Improved patient convenience and compliance due to less frequent drug administration.
- Reduction in fluctuation in steady state levels and therefore better control of disease condition and reduced intensity of local or systemic side effects.
- Increased safety margin of high potency drugs due to better control of plasma levels.
- Maximum utilization of drug enabling reduction in total amount of dose administered.
- Reduction in health care costs through improved therapy, shorter treatment period, less frequency of dosing.
- Despite the several advantages associated with oral controlled drug delivery systems, there are so many disadvantages, which are as follows:
  - Basic assumption is drug should absorb throughout GI tract.

- Limited gastric residence time which ranges from few minutes to 12 hours.
- Drug should not be targeted to specific region of GIT.

The above mention limitation of controlled release can be over come by Gastro retentive system:

It is evident from the recent scientific and patent literature that an increased interest in novel dosage forms that are retained in stomach for a prolonged and predictable period of time exists today in academic and industrial research groups. One of the most feasible approaches for achieving a prolonged and predictable drug delivery profile in the GI tract is to control the gastric residence time (GRT), i.e. Gastro retentive Dosage Forms (GRDFs), will provide us with new and important therapeutic options. These efforts results in Gastro retentive dosage forms (GRDFs) that was designed in large part based on the following approaches:

- Mucoadhesive drug delivery system
- Slowed motility of the GI tract by concomitant administration of drugs or pharmaceutical excipients
- Expansion by swelling or unfolding to a large size which limits emptying of the dosage forms through the pyloric sphincter
- Use of ion-exchange resin which adhere to mucosa
- Modified shape system
- Low density dosage form that is remains buoyant above gastric fluid (Floating Drug Delivery System)
- High density dosage form that is retain in the bottom of the stomach

Good (1976) defined Bioadhesion as the state in which two materials, at least one of which being of biological nature, are held together for an extended period of time by interfacial forces. It is also defined as the ability of a material adheres to a biological tissue for an extended period of time.

The mucoadhesive drug delivery system may include the following:

- Gastrointestinal delivery system.
- Sublingual delivery system.
- Vaginal delivery system.
- Nasal delivery system.
- Ocular delivery system.
- Rectal delivery system.
- Buccal delivery system.

## OVERVIEW ON STOMACH

The stomach is located in the upper left hand portion of the abdomen just below the diaphragm. It occupies a portion of the epigastric and left hydrochondriac region .The main function of the stomach is to store the food temporarily, grind it and then release it slowly into the duodenum. Due to its small surface area, very little absorption takes place from the stomach. It provides a barrier to the delivery of drugs to the small intestine.

Structure: The stomach has four main regions:

- Cardia
- Fundus
- Body
- Pylorus

The main function of Fundus and body is storage, where as Cardia is for mixing or grinding. The Fundus adjuststhe increased volume during eating by relaxation of the

Fundus muscle fibers. The Fundus also exerts a steady pressure on the gastric contents pressing them towards the distal stomach. To pass through the pyloric valves into the small intestine, particles should be the order of 1-2 mm. The antrum does this grinding.

## CONCEPTS

Adhesion can be defined as the bond produced by contact between a pressure sensitive adhesive and a surface.

In biological systems, four types of bioadhesion could be distinguished:

- Adhesion of a normal cell on another normal cell.
- Adhesion of a cell with a foreign substance.
- Adhesion of a normal cell to a pathological cell.
- Adhesion of an adhesive to a biological substance.

For drug delivery purpose, 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. Bioadhesion can be modeled after a bacterial attachment to tissue surfaces, and mucoadhesion can be modeled after the adherence of mucus on epithelial tissue.

## THE MUCUS LAYER: [12, 19]

Mucus is a translucent and viscid secretion, which forms a thin, continuous gel blanket adherent to mucosal epithelial surface. The mean thickness of this layer varies from about 50-450  $\mu\text{m}$  in humans. It is secreted by the goblet cells lining the epithelia or by special exocrine glands with mucus cells acini. The exact composition of the mucus layer varies substantially, depending on the species, the anatomical location and pathological states. However, it has general composition.

**Table1: - Composition of mucus**

Sr. no.	Components	% Amount
1	Water	95
2	Glycoprotein and lipids	0.5-5.0
3	Minerals salts	1
4	Free proteins	0.5-1.0

### Function of mucus layer

The primary functions of the mucus layer are: -

- **Protective:** - Resulting particularly from its hydrophobic.
- **Barrier:** - The role mucus layer as barrier in tissue absorption of drugs and other

substances is well known as it influences the bioavailability of the drugs.

- **Adhesion:** - Mucus has strong cohesive properties and firmly binds to the epithelial cells surface as continuous gel layer.

- **Lubrication:** - An important role of the mucus layer is to keep the mucosal membrane moist.

Continuous secretion of mucus from the goblet cells is necessary to compensate for the removal of mucus layer due to digestion, bacterial degradation and solubilization of mucin molecules.

At physiological pH, the mucus network may carry a significant negative charge because of the presence of sialic acid and sulphate residues and this high charge density due to negative charge contributes significantly to the bioadhesion.

### MUCOADHESIVE POLYMER [12]

There are two broad classes of mucoadhesive polymers: hydrophilic polymer and hydrogels. In the large classes of hydrophilic polymers those containing carboxylic group exhibit the best mucoadhesive properties, poly vinyl pyrrolidone (PVP), Methyl cellulose (MC), Sodium carboxy methylcellulose (SCMC) Hydroxy propyl cellulose (HPC) and other cellulose derivative. Hydrogels are the class of polymeric biomaterial that exhibit the basic characteristics of an hydrogels to swell by absorbing water interacting by means of adhesion with the mucus that covers epithelia i.e.

- Anionic group- Carbopol, Polyacrylates and their crosslinked modifications
- Cationic group- Chitosan and its derivatives
- Neutral group- Eudragit- NE30D etc.

### Characteristics of an Ideal Mucoadhesive Polymer

- The polymer and its degradation products should be nontoxic and should be non absorbable from the GI tract.
- It should be nonirritant to the mucus membrane.
- It should preferably form a strong non covalent bond with the mucin–epithelial cell surfaces.
- It should adhere quickly to most tissue and should possess some site specificity.
- It should allow easy incorporation of the drug and should offer no hindrance to its release.
- The polymers must not decompose on storage or during the shelf life of the dosage form.
- The cost of polymer should not be high so that the prepared dosage form remains competitive.

Robinson and his group using the fluorescence technique concluded that:

- Cationic and anionic polymers bind more effectively than neutral polymers.
- Polyanions are better than polycations in terms of binding/ potential toxicity, and further, that water-insoluble polymers give greater flexibility in dosage form design compared with rapidly or slowly dissolving watersoluble polymers.
- Anionic polymers with sulfate groups bind more effectively than those with carboxylic groups.
- Degree of binding is proportional to the charge density on the polymer.

- Highly binding polymers include carboxy methyl cellulose, gelatine, hyaluronic acid, carbopol, and polycarbophyl.

### Molecular Characteristics

Investigations into polymers with various molecular characteristics have led to a number of conclusions regarding the molecular characteristics required for mucoadhesion. The properties exhibited by a good

Mucoadhesive may be summarized as follows

- Strong hydrogen-bonding groups [–OH, –COOH]
- Strong anionic charges
- Sufficient flexibility to penetrate the mucus network or tissue crevices
- Surface tension characteristics suitable for wetting mucus/ mucosal tissue surface
- High molecular weight

### Factors affecting Mucoadhesion [12, 23]

#### • Polymer related factors:

- Molecular weight
- Concentration of active polymer
- Flexibility of polymer chains
- Special confirmation
- Swelling

#### • Environment related factors:

- pH of polymer - substrate interface
- Applied strength
- Initial contact time

#### • Physiological factors:

- Mucin turns over
- Disease state

### Polymer-Related Factors

#### • Molecular weight

The optimum molecular weight for maximum

bioadhesion depends upon type of mucoadhesive polymer a tissue. It is generally understood that the threshold required for successful bioadhesion is at least 100 000 molecular weight. For example, polyethylene glycol (PEG), with a molecular weight of 20 000, has little adhesive character, whereas PEG with 200 000 molecular weight has improved, and PEG with 400 000 has superior adhesive properties. The fact that mucoadhesiveness improves with increasing molecular weight for linear polymers implies two things:

- interpenetration is more critical for a low-molecular-weight polymer to be a good mucoadhesive, and
- Entanglement is important for high-molecular-weight polymers. Adhesiveness of a nonlinear structure, by comparison, follows a quite different trend. The adhesive strength of dextran, with a high molecular weight of 19 500 000 is similar to that of PEG, with a molecular weight of 200 000. The reason for this similarity may be that the helical conformation of dextran may shield many of the adhesive groups, which are primarily responsible for adhesion, unlike the conformation of PEG.

#### • Concentration of active polymer

There is an optimum concentration for a mucoadhesive polymer to produce maximum bioadhesion. In highly concentrated system, beyond the optimum level, however, the adhesive strength drops significantly because the coiled molecules become separated from the medium so that the chain available for interpenetration becomes limited.

- Flexibility of polymer chains



Chain flexibility is critical for interpenetration and entanglement. As water soluble polymers become cross linked, the mobility of an individual polymer chain decreases and thus the effective length of the chain that can penetrate into the mucus layer decreases, which reduces mucoadhesive strength.

- **Spatial conformation**

Besides molecular weight or chain length, spatial conformation of a molecule is also important. Despite a high molecular weight of 19 500 000 for dextrans, they have adhesive strength similar to that of PEG, with a molecular weight of 200 000. The helical conformation of dextran may shield many adhesively active groups, primarily responsible for adhesion, unlike PEG polymers, which have a linear conformation.

- **Swelling**

Swelling characteristics are related to the mucoadhesive itself and its environment. Swelling depends on the polymer concentration, the ionic strength, and the presence of water. During the dynamic process of bioadhesion, maximum bioadhesion in vitro occurs with optimum water content. Overhydration results in the formation of a wet slippery mucilage without adhesion.

### **Environment-Related Factors**

- **pH of polymer–substrate interface**

pH can influence the formal charge on the surface of the mucus as well as certain ionizable mucoadhesive polymers. Mucus will have a different charge density depending on pH due to the difference in dissociation of functional groups on the carbohydrate moiety and the amino acids of the polypeptide backbone. Some

studies had shown that the pH of the medium is important for the degree of hydration of cross-linked polycyclic acid, showing consistently increased hydration from pH 4 through pH 7, and then a decrease as alkalinity or ionic strength increases, for example polycarbophil does not show a strong mucoadhesive property above pH 5 because uncharged, rather than ionized, carboxyl group reacts with mucin molecule, presumably through

Numerous hydrogen bonds. However, at higher pH, the chain is fully extended due to electrostatic repulsion of the carboxylate anions.

- **Applied strength**

To place a solid mucoadhesive system, it is necessary to apply a defined strength. Whatever the polymer, poly (acrylic acid/divinyl benzene) or carbopol 934, the adhesion strength increases with the applied strength or with the duration of its application, up to an optimum. The pressure initially applied to the mucoadhesive tissue contact site can affect the depth of interpenetration. If high pressure is applied for a sufficiently long period of time, polymers become mucoadhesive even though they do not have attractive interactions with mucin.

- **Initial contact time**

Contact time between the mucoadhesive and mucus layer determines the extent of swelling and interpenetration of the mucoadhesive polymer chains. More mucoadhesive strength increases as the initial contact time increases.

### **Physiological Factors**

- **Mucin turnover**

The natural turnover of mucin molecules from the mucus layer is important for at least two reasons. Firstly, the mucin turnover is expected

to limit the residence time of the mucoadhesives on the mucus layer. No matter how high the mucoadhesive strength, they are detached from the surface due to mucin turnover. The turnover rate may be different in the presence of mucoadhesives, but no information is available on this aspect. Secondly, mucin turnover results in substantial amounts of soluble mucin molecules. These molecules interact with mucoadhesives before they have chance to interact with the mucus layer. Surface fouling is unfavorable for mucoadhesion to the tissue surface. Mucin turnover may depend on the other factors such as the presence of food. The gastric mucosa accumulates secreted mucin on the luminal surface of the tissue during the early stages of fasting. The accumulated mucin is subsequently released by freshly secreted acid or simply by the passage of ingested food; the exact turnover rate of the mucus layer remains to be determined. Lehr et al. calculated a mucin turnover time of 47–270 min. The ciliated cells in the nasal cavity are known to transport the mucus to the throat at the rate of 5 mm/min. The mucociliary clearance in the tracheal region has been found to be at the rate of 4–10 mm/min.

- **Disease state**

The physicochemical properties of the mucus are known to change during disease conditions such as the common cold, gastric ulcers, ulcerative colitis, cystic fibrosis, bacterial, and fungal infections of female reproductive tract, and inflammatory conditions of the eye. The exact structural changes taking place in mucus under these conditions are not clearly understood. If mucoadhesives are to be used in the disease

states, the mucoadhesive property needs to be evaluated under the same conditions.

## EVALUATION OF MUCOADHESIVE TABLETS

All the prepared mucoadhesive tablets were evaluated for following parameters.

- **Hardness**

Hardness was measured using Monsanto hardness tester. For each batch three tablets were tested.

- **Friability**

Twenty tablets were weighed and placed in the Roche friabilator and apparatus was rotated at 25 rpm for 4 minutes. After revolutions the tablets were dusted and weighed again. The percentage friability was measured using the formula,

$$\% F = \{1 - (W_o/W)\} \times 100$$

Where, % F = friability in percentage

W<sub>o</sub> = Initial weight of tablet

W = weight of tablets after revolution

- **Weight Variation<sup>26,28</sup>:**

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviate from the average weight by more than the percentage shown in Table No.5 and none deviate by more than twice the percentage shown.

**Table – 5 Percentage deviation allowed under weight variation test.**

Average weight of tablet (mg)	Percentage deviation
130 or less	10
130-324	7.5
More than 324	5

- **Thickness:**

Three tablets were selected randomly from each batch and thickness was measured by using vernier calliper. [26]

- **Mucoadhesive Strength:**

Mucoadhesive strength of the tablet was measured on the modified physical balance. The design used for measuring the mucoadhesive strength was shown in Fig. No.5. The apparatus consist of a modified double beam physical balance in which the right pan has been replaced by a glass slide with copper wire and additional weight, to make the right side weight equal with left side pan. A Teflon block of 3.8 cm diameter and 2 cm height was fabricated with an upward portion of 2 cm height and 1.5 cm diameter on one side. This was kept in beaker filled with buffer media 0.1N HCl pH 1.2, which was then placed below right side of the balance. [29, 30]

Goat or rat stomach mucosa was used as a model membrane and buffer media 0.1N HCl pH 1.2 was used as moistening fluid. The goat or rat stomach mucosa was obtained from local slaughter house and kept in a Krebs buffer during transportation. The underlying mucous membrane was separated using surgical blade and wash thoroughly with buffer media 0.1N HCl pH 1.2. It was then tied over the protrusion

in the Teflon block using a thread. The block was then kept in glass beaker. The beaker was filled with phosphate buffer media 0.1N HCl pH 1.2 up to the upper surface of the goat stomach mucosa to maintain stomach mucosa viability during the experiments.

The one side of the tablet was attached to the glass slide of the right arm of the balance and then the beaker was raised slowly until contact between goat mucosa and mucoadhesive tablet was established. A preload of 10 mg was placed on the slide for 5 min (preload time) to established adhesion bonding between mucoadhesive tablet and goat or rat stomach mucosa. The preload and preload time were kept constant for all formulations. After the completion of preload time, preload was removed from the glass slide and water was then added in the plastic bottle in left side arm by peristaltic pump at a constant rate of 100 drops per min. The addition of water was stopped when mucoadhesive tablet was detached from the goat or rat stomach mucosa.

The weight of water required to detach mucoadhesive tablet from stomach mucosa was noted as mucoadhesive strength in grams. From the mucoadhesive strength following parameter was calculated.

**Force of adhesion (N) = Mucoadhesive strength × 9.81 1000**

**Bond strength (N/m<sup>2</sup>) = Force of adhesion (N) / Surface area of tablet (m<sup>2</sup>)**

- **Swelling index**

Swelling of tablet excipients particles involves the absorption of a liquid resulting in an increase in weight and volume. Liquid uptake by the particle may be due to saturation of capillary

spaces within the particles or hydration of macromolecule. The liquid enters the particles through pores and bind to large molecule, breaking the hydrogen bond and resulting in the swelling of particle. The extent of swelling can be measured in terms of % weight gain by the tablet. [31, 32, 33, 35]

#### **Method:**

For each formulation batch, one tablet was weighed and placed in a beaker containing 200 ml of buffer media. After each interval the tablet was removed from beaker and weighed again up to 8 hours. The swelling index was calculated using following formula.

$$\text{Swelling Index (S.I.)} = (W_t - W_0) / W_0$$

Where, S.I. = Swelling index

$W_t$  = Weight of tablet at time  $t$

$W_0$  = Weight of tablet before placing in the beaker

#### • **In Vitro Release Study:**

Standard USP or IP dissolution apparatus have been used to study in vitro release profile using both basket and rotating paddle. In vitro release rate study of mucoadhesive tablet of was carried out using the Apparatus 2 (Basket apparatus) method. Place the tablet in a dry basket at the beginning of each test. Lower the Basket before rotation operates the apparatus immediately at 50 rpm. Medium used for release rate study was 900ml 0.1 N HCl during the course of study whole assembly was maintained at  $37 \pm 0.5$  oC. Withdraw a 5 ml of sample at sprcific time interval and replaced with 5 ml of fresh dissolution medium. The withdrawn samples were dilute with dissolution medium and then filter it with whattman filter paper and assayed

.The % release of drug was calculated .The observations for different batches are shown in succeeding Tables. The percentage release of drug with respect to time for each batch, are graphically show. [12, 29]

### **STABILITY STUDIES**

The success of an effective formulation can be evaluated only through stability studies. The purpose of stability testing is to obtain a stable product which assures its safety and efficacy up to the end of shelf life at defined storage conditions and peak profile. [29]

#### **Advantages:** [12, 34, 35, 36]

- A prolonged residence time at the site of action or absorption.
- A localization of the dosage form at a specific site.
- An increase in the drug concentration gradient due to the intestine contact of the drug particles
  - with the mucosal surface,
- A direct contact with intestinal cells, which is the step earlier to particle absorption.

### **Measurement of the Residence Time/In Vivo Techniques**

Measurements of the residence time of mucoadhesives at the application site provide quantitative information on their mucoadhesive properties. The GI transit times of many mucoadhesive preparations have been examined using radioisotopes and the fluorescent labeling techniques.

### GI Transit using Radio-Opaque Tablets

It is a simple procedure involving the use of radio-opaque markers, e.g. barium sulfate, encapsulated in mucoadhesive tablets to determine the effects of mucoadhesive polymers on GI transit time. Feces collection (using an automated feces collection machine) and X-ray inspection provide a non-invasive method of monitoring total GI residence time without affecting normal GI motility. Mucoadhesives labeled with Cr-51, Tc-99m, In-113m, or I-123 has been used to study the transit of the tablets in the GI tract. [34]

### CONCLUSION

Mucoadhesive tablets offer unique carrier system for many pharmaceuticals and can be tailored to adhere to any mucosal tissue, including those found in oral cavity and gastrointestinal tract. The mucoadhesive tablets can be used not only for controlled release of the drugs to specific sites in body. Recent advances in medicine have envisaged the development of polymeric drug delivery systems for protein/peptide drugs and gene therapy. These challenges put forward by the medicinal advances can be successfully met by using

increasingly accepted polymers, e.g. HPMC, polyacrylates, carbopol and its derivatives, polyphosphazenes, etc. Many studies have already been undertaken for exploring the prospects of mucoadhesive tablets in local action in stomach. Although significant advances have been made in the field of mucoadhesives, there are still many challenges ahead in this field. Of particular importance is the development of universally acceptable standard evaluation methods and development of newer site directed polymers. Efforts have been initiated on these lines in the form of novel techniques for evaluation of mucoadhesive strength of tablets to specific cell types. Polymeric science needs to be explored to find newer mucoadhesive polymers with the added attributes of being biodegradable, biocompatible, mucoadhesive for specific cells or mucosa and which could also function as enzyme inhibitors for the successful delivery of proteins and peptides. A multidisciplinary approach will therefore be required to overcome these challenges and to employ mucoadhesive tablets as a cutting edge technology for site of stomach controlled release drug delivery of new as well as existing drugs.

### REFERENCES

1. A Hoffman *Pharmacodynamic aspect of sustained release preparations. Adv Drug Del Rev* 1998; 33: 185–99.
2. SJ Hwang, H Park, K Park. *Gastric retentive drug-delivery systems. Crit Rev Ther Drug Carrier Sys* 1998;15: 243–84.
3. AHoffman,D Stepensky. *Pharmacodynamic aspects of modes of drug administration for optimization of drug therapy. Crit Rev Ther Drug Carrier Sys* 1999;16: 571–639.
4. AA Deshpande, CT Rhodes, NH Shah, AW Malick. *Controlled-release drug delivery systems for prolonged gastric residence: an overview. Drug Dev Ind Pharm* 1996; 22: 31–39.
5. BN Singh, KH Kim. *Floating drug delivery systems: an approach to oral controlled drug*

- delivery via gastric retention. *J Cont Rel* 2000; 63: 235–59.
6. AJ Moes. *Gastroretentive dosage forms. Crit Rev Ther Drug Carrier Syst.* 1993; 10: 143–95.
  7. JK Vasir, K Tambwekar, S Garg. *Mucoadhesive tablets as a controlled drug delivery system. International Journal of Pharmaceutics* 200; 255: 13-32.
  8. AF Stockwell, SS Davis, SE Walker. *In-vitro evaluation of alginate gel systems. J.Control.release* 1986; 3: 167 – 175.
  9. J Timmermanns, A Moes . *How well do floating dosage forms float?. Int.J.Pharm.* 1990; 62(3): 207 – 216.
  10. PG Yeole, S Khan, VF Patel. *Floating drug delivery systems: Need and development. Indian.J.Pharm.Sci.* 2005; 67(3): 265 – 272.
  11. R Groning G Henu. *Dosage forms with controlled gastrointestinal passage-studies on the absorption of nitrofurantoin Int J Pharm .1989; 56: 111-116.*
  12. NK .Jain. *Controlled release and Novel Drug Delivery. 1st edition.CBS publishers and Distributors New Delhi.*1997; 353-370.
  13. DM. Brahmankar SB Jaiswal. *.Biopharmaceutics and Pharmacokinetics A treatise.*1995; 337-371.
  14. RJ Good, J. Adhesion, 1976; 8:1-15.
  15. NA Peppas and PA Buri. *J controlled release;* 1985; ;, 257.
  16. MA. Longer and JR Robinson, *Pharm.Int,* 1987, 7,114.
  17. S Desai. *A Novel Floating Controlled release Drug Delivery system based on Dried Gel Matrix Network.*
  18. Jimenez-Castellanous. *J.Pharm.* 1993;12: 246
  19. Gayot, *J.pharm. Belg,* 1985; 40:332
  20. Robert and P.Buri, *Phar. Acta Helv.* 1986; 61:210.
  21. H Park and JR Robinson, “*Mechanism s of mucoadhesion og polyacrylic acid and hydrogels*”, *Pharm. Res.*, 1987;4:457-464.
  22. G. Ponchel, F. Touchard, , D. Duchene, and N. A. Peppas, “*Bioadhesive analysis of controlled res. systems, I. fracture and interpenetration analysis in poly acrylic acid containing systems*”, *J. Control. Res.* 1987;5:129-141.
  23. H. W. Hui and J. R. Robinson, “*Ocular delivery of progesterone using bioadhesive polymer*”, *Int. J. Pharm.*, 1985;26:203-213.
  24. A Ahuja, RK Khar, J Ali. *Mucoadhesive drug delivery systems, Drug Development and industrial pharmacy,* 1997; 23 (5):489-515.
  25. D Chickering, J Jacob, E Mathiowitz. *Poly (fumaric-cosebacic) microspheres as oral drug delivery systems. Biotechnol. Bioeng.* 1996;52:96–101
  26. Leon Lachman, Herbert A.Lieberman, Joseph L. Kangi. *The Theory and Practice of Industrial Pharmacy,* 1991; 296-302.
  27. S Gilbert, R Neil, L Lachman, HA Liberman et al, editors. *The theory and practice of Industrial pharmacy, third edition, Mumbai; Varghese Publishing House;* 1990; 88: 299.
  28. “*United States Pharmacopoeia*”, xxiv NF 19, Rockville: *United States Pharmacopoeia Convention;* 2000; 23(8):8-9.
  29. VN Deshmukh, JK.Jadhav, DM sakarkar. *Formulation and in vitro evaluation of theophylline anhydrous Bioadhesive tablets; Asian journal of pharmaceutics;* 2009, 3, 54-58.
  30. Gupta A, Garg S, and Khar R, *Measurement of bioadhesive strength of mucoadhesive buccal tablets: Design of in vitro assembly. Indian Drug* 1992; 30: (15)2-5.
  31. N.G.Sonani, S. P. Hiremath, F.S. Dasankoppa , V.G. Jamakandi, S.A.Steenivas.*Design and evaluation of gastroretentive mucoadhesive Cephalexin tablets. Pharmaceutical development and technology.* July 2009; on line.
  32. VM. Patel, G. prajapati, M. patel. *Mucoadhesive Bilayer tablets of Propranolol Hydrochloride. AAPS Pharmasci tech,* 2007;8: 234-242.

33. C Margeta, BS Sachin, B Debjit, B Bhowmik, B Jayakar. *Formulation and evaluation of Controlled release mucoadhesive oral tablet of Clarithromycine. Der pharmacia Lettre*; 2009; 1, 83-91.

34. JL Richardson, TI Armstrong,. *Vaginal delivery of calcitonin by hyaluronic acid formulations. In:*

*Mathiowitz E, Chickering DE, Lehr CM, editors. Mucoadhesive Drug Delivery Systems—Fundamentals, Novel Approaches and Development '98. New York: Marcel Dekker; 1999; 5:63–99.*

