Mucoadhesion is a topic of current interest in the design of drug delivery systems. The Gastrointestinal Mucosaadhesive delivery system prolong the residence time of the dosage form at the site of absorption and facilitate an intimate contact of the dosage form with the underline absorption surface and thus contribute to improved and/or better therapeutic performance of the drug. The process of mucoadhesion involving a polymeric drug delivery platform is a complex one that includes wetting, adsorption and interpenetration of polymer chains amongst various other processes. There are various factor influences the Gastro-Intestinal retention and mucoadhesion. This paper describes some effort to increase the residence time of drug dosage forms in GI tract, by gastroretentive units and bioadhesive gastrointestinal patches. Several gastrointestinal patch systems provide bioadhesion, drug protection and unidirectional release, This combination of function could improve the overall oral bioavailability.

Key words: Intestinal transit time, Mucoadhesive Drug Delivery System, GI Patches

INTRODUCTION

Historically, oral drug administration has been the predominant route for drug delivery. During the past two decades, numerous oral delivery systems have been developed to act as drug reservoirs from which the active substance can be released over a defined period of time at a predetermined and controlled rate. From a pharmacokinetic point of view, the ideal sustained release dosage form is not just to prolong the delivery of drugs for 24hrs but also to prolong the presence of dosage forms in the stomach or intestine. Gastro-intestinal dosage forms through local drug release will greatly enhance the pharmacotherapy of the GIT leading to high drug concentrations at the gastric or intestinal mucosa, which are sustained over a long period of time. Several times a day according to a complicated regimen and which frequently is unsuccessful as a consequence of insufficient patient compliance, could possibly be achieved more reliably using gastro-intestinal dosage form. Finally, gastrointestinal dosage form can be used as potential delivery system for drugs with narrow absorption windows.

GASTRORETTENTIVE DRUG DELIVERY SYSTEM: 3-4

The relatively short gastric emptying time in humans, which normally averages 2-3 hrs through the major absorption zone (stomach or upper part of the intestine), can result in incomplete drug release from the drug delivery system leading to diminished efficiency of the administered dose. Thus, localization of a drug delivery system in a specific region of the GIT offers numerous advantages, especially for drugs having narrow absorption window. The intimate contact of the dosage form with the absorbing membrane has the potential to maximize drug absorption and may also influence the rate of drug absorption. These considerations have led to the development of oral sustained release dosage forms possessing gastric or intestinal retention potential. The primary concern in the development of once daily oral sustained release dosage form is not just to prolong the delivery of drugs for 24hrs but also to prolong the presence of dosage forms in the stomach or intestine.

Gastro-intestinal dosage forms through local drug release will greatly enhance the pharmacotherapy of the GIT leading to high drug concentrations at the gastric or intestinal mucosa, which are sustained over a long period of time. The GIT is a continuous muscular tube, extending from the mouth to the anus, which functions to take in nutrients and eliminate waste by such physiological processes as secretion, motility, digestion, absorption and excretion. The organization of the GIT, from stomach to large intestine, is shown in Fig.1. The stomach is a J-shaped enlargement of the GIT whose function is to store and mix food with gastric secretions before emptying its load (chyme) through the pyloric sphincter and into the small intestine at a controlled rate suitable for digestion and absorption. When empty, the stomach occupies a volume of about 50 ml, but this may increase to as much as 1 liter when full. Table 1 contains some salient features of Upper GIT.

Table1. Salient Features of Upper Gastrointestinal Tract 1

<table>
<thead>
<tr>
<th>Section</th>
<th>Length (m)</th>
<th>Transit time (h)</th>
<th>pH</th>
<th>Microbial count</th>
<th>Absorbing surface area (m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>0.2</td>
<td>Variable</td>
<td>1-3</td>
<td>&lt;103</td>
<td>0.1</td>
</tr>
<tr>
<td>Small Intestine</td>
<td>6-10</td>
<td>3 ± 1</td>
<td>5-7.5</td>
<td>100 – 1010</td>
<td>120-200</td>
</tr>
</tbody>
</table>

The walls of the GIT, from stomach to large intestine, have the same basic arrangement of tissues, the different layers, from outside to inside, comprising serosa, longitudinal muscle, intermuscular plane, circular muscle, submucosa, muscularis mucosae, lamina propria and epithelium. In addition to longitudinal and circular muscle, the stomach has a third muscle layer known as the "oblique muscle layer", which is situated in the proximal stomach, branching over the fundus and higher regions of the gastric body. The different smooth muscle layers are responsible for performing the motor functions of the GIT, i.e. gastric emptying and intestinal transit. 7

The GI tract consists of four concentric layers: Mucosa, Submucosa, Muscularis externa (the external muscle layer), Adventitia or serosa. The mucosa is the innermost layer of the gastrointestinal tract that is surrounding the lumen, or space within the tube. This layer comes in direct contact with food (or bolus), and is responsible for absorption and secretion, important processes in digestion.

The mucosa can be divided into:
- Epithelium
- Lamina propria
- Muscularis mucosae

The mucosa are highly specialized in each organ of the gastrointestinal tract, facing a low pH in the stomach, absorbing a multitude of different substances in the small intestine, and also absorbing specific quantities of water in the large intestine. Reflecting the varying needs of

1. UN.1
2. Not Available in this Section.
5. Rahmat et al., 2003.
Van-der-Waals bonds is attracted to other electronegative atoms. The hydrogen can therefore be thought of as being atoms such as oxygen, fluorine or nitrogen, carries a slight positively charge and is therefore hydrogen bonded structures, which lowers the system entropy.

Hydrophobic bonds occur when non-polar groups only appear to be attracted to each other) that occur when non-polar interactions to form a strong bond (e.g. in a salt crystal).

According to Good following way: For adhesion to occur, molecules must bond across the interface. These bonds can arise in the following way:

1) Adhesion of a normal cell to another normal cell.
2) Adhesion of a cell with a foreign substance.
3) Adhesion of a normal cell to a pathological cell.
4) Adhesion of an adhesive to a biological substrate.

For adhesion to occur, molecules must bond across the interface. These bonds can arise in the following way: 12

1) Ionic bonds—where two oppositely charged ions attract each other via electrostatic interactions to form a strong bond (e.g. in a salt crystal).
2) Covalent bonds—where electrons are shared, in pairs, between the bonded atoms in order to fill the orbital in both. These are also strong bonds.
3) Hydrogen bonds—here a hydrogen atom, when covalently bonded to electronegative atoms such as oxygen, fluorine or nitrogen, carries a slight positively charge and is therefore is attracted to other electronegative atoms. The hydrogen can therefore be thought of as being shared, and the bond formed is generally weaker than ionic or covalent bonds.
4) Van-der-Waals bonds—these are some of the weakest forms of interaction that arise from dipole–dipole and dipole-induced dipole attractions in polar molecules, and dispersion forces with non-polar substances.

Hydrophobic bonds—more accurately described as the hydrophobic effect, these are indirect bonds (such groups only appear to be attracted to each other) that occur when non-polar groups are present in an aqueous solution. Water molecules adjacent to non-polar groups form hydrogen bonded structures, which lowers the system entropy.

Mucus: structure, function and Composition

Mucus is a complex viscus adhesive secretion which is synthesized by specialized goblet cells. These goblet cells are glandular columnar epithelium cells and line all organs that are exposed to the external environment. The mean thickness of this layer varies from about 50–450 µm in humans. The exact composition of the mucus layer varies substantially, depending on the species, the anatomical location and pathological states. However, it has general composition:

Composition of mucus

<table>
<thead>
<tr>
<th>Component</th>
<th>% amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>95.0</td>
</tr>
<tr>
<td>Glycoprotein &amp; lipids</td>
<td>0.5 - 5.0</td>
</tr>
<tr>
<td>Mineral salts</td>
<td>1.0</td>
</tr>
<tr>
<td>Free proteins</td>
<td>0.5 - 1.0</td>
</tr>
</tbody>
</table>

From an engineering point of view, mucus is an outstanding water-based lubricant whose properties are extensively exploited within nature.

Function of mucus layer

The primary functions of the mucus layer are:

1) 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 influence the bioavailability of the drug Adhesion - Mucus has strong cohesionial 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.

MUCOADHESIVE SYSTEMS

Mucosal adhesion is defined as attractive interactions at the interface between a pharmaceutical dosage form and a mucosal membrane. Various administration routes, such as ocular, nasal, buccal and gingival, gastrointestinal (oral), vaginal and rectal, can make mucosal adhesion drug delivery systems attractive and flexible in dosage form development. The advantages associated with the use of mucosadhesives in drug delivery include increased dosage form residence time, improved drug bioavailability, and reduced administration frequency, simplified administration of a dosage form and termination of a therapy as well as the possibility of targeting particular body sites and tissues.

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

In case of mucosal adhesion, the biological tissue is the mucous membrane. For mucosal adhesion to occur, a succession of phenomena is required.

Mucosal adhesion stages 10

1) An intimate contact between a bioadhesive and a membrane.
2) Penetration of the bioadhesive into the crevice of the tissue surface.
3) Mechanical interlocking between mucin and polymer.

Types of Mucosal adhesion 11

In biological systems, four types of Mucosal adhesion can be distinguished:

1) Adhesion of a normal cell on another normal cell.
2) Adhesion of a cell with a foreign substance.
3) Adhesion of a normal cell to a pathological cell.
4) Adhesion of an adhesive to a biological substrate.

Examples of some Mucosal adhesives

<table>
<thead>
<tr>
<th>Natural/Semi-synthetic</th>
<th>Synthetic</th>
<th>Biocompatible</th>
<th>Bioadgradable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na alginate</td>
<td>Pectin,</td>
<td>Ester of haluronic acid,</td>
<td>Poly(lactides),</td>
</tr>
<tr>
<td>Agarose</td>
<td>Tragacanth,</td>
<td>Polyvinyl acetate,</td>
<td>Poly(caprolactones),</td>
</tr>
<tr>
<td>Chitosan</td>
<td>Carragenan,</td>
<td>Ethylene glycol.</td>
<td>Poly(caprolactones),</td>
</tr>
<tr>
<td></td>
<td>Polyamides,</td>
<td></td>
<td>Poly(carboxylic),</td>
</tr>
<tr>
<td></td>
<td>Poly(vinyl) ethers,</td>
<td></td>
<td>Poly(carboxylic),</td>
</tr>
<tr>
<td></td>
<td>PMMA,</td>
<td></td>
<td>Poly(alkyl cyanoacrylates),</td>
</tr>
<tr>
<td></td>
<td>HPC,</td>
<td></td>
<td>Poly(alkyl cyanoacrylates),</td>
</tr>
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<td></td>
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<td></td>
<td>Poly(alkyl cyanoacrylates),</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Poly(amide),</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Poly(amide),</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Poly(amide),</td>
</tr>
</tbody>
</table>

Factors affecting mucosaladhesion:

1) Polymer Related Factors: 20

a) Molecular weight - The interpenetration of polymer molecules into the mucus layer is variable, for low molecular weight polymers penetration is more than high molecular weight polymers because entanglements are favored in high molecular weight polymers.

b) Concentration of active polymer: For solid dosage forms such as tablets, the higher the concentration of polymer, the stronger the bioadhesion force.

c) Spatial Conformation: Bioadhesive force is also dependent on the conformation of polymers, i.e., helical or linear. The helical conformation of polymers may shield many active groups, primarily responsible for adhesion, thus reducing the mucosaladhesive strength of the polymer.

d) Chain flexibility of polymer: Chain flexibility is important for interpenetration and enlargement. As water-soluble polymers become more and more cross linked, the mobility of the individual polymer chain decreases, also as the cross linking density increases, the effective length of the chain which can penetrate into mucus decrease even further and mucosaladhesive strength is reduced.

e) Degree of Hydration: Another important factor affecting the mucosaladhesive strength of polymeric components is the degree of hydration. In this respect many polymers will exhibit adhesive properties under...
conditions where the amount of water is limited. However in such a situation, adhesion is thought to be a result of a combination of capillary attraction and osmotic forces between the dry polymer and the wet mucosal surface which act to dehydrate and strengthen the mucus layer. Although this kind of “sticking” has been referred to as mucoadhesion it is important to clearly distinguish such processes from “wet-on-wet” adhesion in which swollen mucoadhesive polymers attach to mucosal surfaces. Hydration is essential for the relaxation and interpenetration of polymer chains, excess hydration could lead to decreased mucoadhesion and/or retention due to the formation of slippery mucilage. In this situation cross linked polymers that only permit a certain degree of hydration may be advantageous for providing a prolonged mucoadhesive effect.\textsuperscript{20}

f) Functional Group Contribution:
The attachment and bonding of bioadhesive polymers to biological substrates occurs mainly through interpenetration followed by secondary non-covalent bonding between substrates. Given that secondary bonding mainly arises due to hydrogen bond formation, it is well accepted that mucoadhesive polymers possessing hydrophilic functional such as, carboxyl (COOH), hydroxyl (OH), amide (NH\textsubscript{2}) and sulphate groups (SO\textsubscript{4}H) may be more favorable in formulating targeted drug delivery platforms. Typically, physical entanglements and secondary interactions (hydrogen bonds) contribute to the formation of a strengthened network; therefore polymers that exhibit a high density of available hydrogen bonding groups would be able to interact more strongly with mucin glycoproteins.\textsuperscript{21}

2) Environmental – Related Factors:\textsuperscript{22-25}

a) pH: pH influences the charge on the surface of both mucus and polymers. Mucus will have a different charge density depending on pH, because of difference in dissociation of functional groups on carbohydrate moieties and amino acids of the polypeptide backbone, which may affect adhesion.

b) Applied strength: To place a solid bioadhesive system, it is necessary to apply a defined strength. Whenever the polymer may be the adhesion strength of those polymers increases with the increase in the applied strength.

c) Initial contact time: The initial contact time between mucoadhesive and the mucus layer determines the extent of swelling and the interpenetration of polymer chains. The mucoadhesive strength increases as the initial contact time increases.

d) Selection of the model substrate surface: The handling and treatment of biological substrates during the testing of mucoadhesive is an important factor, since physical and biological changes may occur in the mucus gels or tissues under the experimental conditions.

3) Swelling

Swelling is the swelling characteristic is related to the polymer itself, and also to its environment. Interpenetration of chains is easier as polymer chains are disentangled and free of interactions. More the swelling of polymeric matrix higher the adhesion time of polymers.

4) Physiological variables:
Mucin turnover and disease state of mucus layer are physiological variables, which may affect bioadhesion.

RECENT ADVANCEMENT IN MUCAADHESIVE POLYMERS\textsuperscript{30}
Recently, a novel promising strategy to imp-rove mucoadhesion has been introduced into the pharmaceutical literature. The most com- monly bridging structure in biological sys-tems, the disulfide bond, is thereby utilized to improve adhesion of polymeric carrier systems to mucosal membranes. Thiolated polymers, designated as thiomers, are believed to interact with cysteine-rich subdomains of mucous glyco- proteins forming disulfide bonds between the mucoadhesive polymer and the mucus layer.

Approaches to Gastro-intestinal drug delivery system
Two types of Approaches are mainly used:

1) GASTRORETTENTIVE DRUG DELIVERY SYSTEM

2) INTESTINAL DRUG DELIVERY SYSTEM

Mucoadhesive Tablets
Mucoadhesive micro/nanoparticles


Fig. 2: interaction of mucoadhesive drug delivery system with mucous layer

Fig. 3: Adhesion of polymer & mucin molecules through hydrogen bonding.

Tablets
Mucoadhesive tablet have potential to be used for controlled release drug delivery but coupling of mucoadhesive properties to tablet has additional advantages. Mucoadhesive tablet can be tailored to adhere to any mucosal tissue found in GIT, thus offering opportunities of localized as well as systemic controlled release of drug.

Girish et al.\textsuperscript{24}, developed a bilayer bioadhesive drug delivery system exhibiting sufficient bioadhesion to prolong residence in the stomach using osoglibizone maleate as a model drug. Granules and tablets were characterized using the official method. The in-vitro drug release, buoyancy lag-time, detachment force and swelling index were evaluated. The in-vitro drug release from the tablet was controlled by the amount of HPMC in the sustained release layer.

Singh et al.\textsuperscript{27}, designed oral controlled release mucoadhesive compressed hydrophilic matrices of atenolol and optimize the drug release profile and bioadhesion using response surface methodology. Tablets were prepared by direct compression and evaluated for bioadhesive strength and in-vitro dissolution parameters. Carbopel 934P and sodium carboxymethylcellulose were taken as the independent variables.

Madgalkar et al.\textsuperscript{28}, prepared a solid dispersion of itraconazole with Eudragit E100 by spray-drying method to improve dissolution. Trilayered mucoadhesive tablet was prepared, with inner core containing solid dispersion of the drug and with carbopol and HPMC sandwiched between two layers of hydrosoluble mucoadhesive polymer mixture of carbopol and hydroxy propyl methyl cellulose (HPMC). Amounts of Carbopel 934P (CP) and Methocel K4M (HPMC) were varied in the outer coat around the solid dispersion.

Micro and/or Nanoparticles
Despite the limited loading capacity of drug, bioadhesive micro- and/or nanoparticles have been widely investigated for three major features:
1. Immobilization of particles on the mucosal surface by adhesion after modification of surface properties via bioadhesive polymers.
2. Very large specific surface between the dosage forms and the oral mucosa.
3. Sustained release of entrapped drug, leading to higher absorption

Wang et al.\textsuperscript{29}, prepared a new positively charged biodegradable microspheres using laminated gelatin by surfactant free emulsification in olive oil, followed by a cross-linking reaction with glutaraldehyde. With the increase of glutaraldehyde concentration, the amino group content of the microspheres decreased accordingly. The influence of glutaraldehyde concentration, cross-linking reaction time, drug-loading patterns, and type of release media on the in-vitro release characteristics of amoxicillin from the microspheres was investigated.
Umamaheshwari et al.31-34, designed a mucoadhesive gliadin nanoparticles (GNP) containing amoxicillin and to evaluate their effectiveness in eradicating H.pylori. GNP bearing amoxicillin (AGNP) was prepared by desolvation method. The effect of pro-cess variables such as gliadin concentration and initial drug loading on particle size, shape, percent payload, percent entrapment efficiency, in-vitro release profile, and mucoadhesive property of GNP was assessed. Patel et al.35-37, formulate and systematically evaluate in-vitro and in-vivo performances of mucoadhesive amoxicillin microspheres for the potential use of treating gastric and duodenal ulcers, which were associated with Helicobacter pylori (H. pylori). Amoxicillin mucoadhesive microspheres containing chitosan as mucoadhesive polymer were prepared by simple emulsification phase separation technique using glutaraldehyde as a cross-linking agent. Microspheres were discrete, spherical, free flowing and also showed high percentage drug entrapment efficiency.

Rajnikanth et al.38, prepared a stomach-specific drug delivery system for controlled release of clarithromycin for eradication of H.pylori. Bioadhesive microspheres of clarithromycin (FBMC) were prepared by emulsification-solvent evaporation method using ethylcellulose as matrix polymer and Carbopol 934P as mucoadhesive polymer. The prepared microspheres were subjected to evaluation for particle size, incorporation efficiency, in-vitro buoyancy, in-vitro mucoadhesion and in-vitro drug release characteristics.

2) INTESTINAL DRUG DELIVERY SYSTEM
These are the systems which can remain in Intestinal region for several hours and prolongs the intestinal transit time. Prolonged transit improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to proximal small intestines.

Mucoadhesive GI patch
One of the proposed approaches for inducing greater levels of absorption and stability at the intestinal epithelium is the use of a multilayered patch system. Patches comprise layers of thin, flexible membranes: an impermeable backing; a drug reservoir; a rate-controlling membrane; and an adhesive. When the patch is applied, the drug flows through the skin into the bloodstream at a rate regulated by the membrane that is preprogrammed to keep the drug at an effective level.

From a technological standpoint, these protective, rate-controlling and adhesive properties are also ideal for oral dosage forms intended for delivery to the intestinal mucosa. This review describes several GI patch systems that have three key attributes:
(i) Bioadhesive properties for retention of the dosage form
(ii) Controlled drug release
(iii) Unidirectional release towards the intestinal epithelium

Figures 4-6: SEM images of microspheres and microsphere patch designs

Following types of patch have been found useful for Intestinal drug delivery:
A) Gastrointestinal-mucoadhesive patch system 36-37
This system consists of four layers:
(i) A backing layer made of a water insoluble polymer to protect protein drugs from en-zymatic hydrolysis.
(ii) A surface layer made of a polymer sensitive to intestinal pH.
(iii) A drug-carrying middle layer.
(iv) An adhesive layer between the middle and surface layers to generate a high con-centration gradient between the patch and intestinal enterocytes (Figure 5).

The first example of this patch system for oral drug delivery was GI – mucoadhesive patch system (GI-MAPS) developed by Eamtrakarn et al.38-40. The Backing layer of ethyl cellulose was prepared by Solvent evaporation. The middle layer, a cellulose membrane was loaded by wetting with a solution containing a model drug [e.g. fluorescein or granulocyte-colony-stimulating factor (G-SCF)] and then dried and attached to the backing layer by thermal bonding.

The pH-sensitive surface layer was prepared using one of three polymers – hydroxypropylmethylcellulose (HP-55), Eudragit L100 or Eudragit S100 (Rohm). The mucoadhesive layer, an aqueous solution of carbosolvin polymer [Carbopol] and polyethylene glycol 400, was spread uni- formly on the surface of the pH-sensitive layer and then attached to the middle layer. The four-layered film was cut into smaller pieces (0.5 mm in diameter for rat studies and 3.0 mm in diameter for dog studies) and treated with micro-

pulverized stearic acid and magnesium silicate to cover the edges of the films to prevent patch agglutination.

B) Drug-in-adhesive patch
This was designed mainly to increase the loading dose. The reworked patch system consisted of three layers:

(i) A backing layer of ethylcellulose
(ii) An enteric polymer membrane of HP-55
(iii) A new drug-carrying layer, based on Carbopol, loaded with 30 mg of fluorescein or fluorescein-dextran as a model drug

Eamtrakarn et al.41-43 redesigned the intestinal patch with an increased loading space and without the adhesive layer. The three-layer preparation was heat sealed and cut into patches 3 mm in diameter. As a reference, the patches were compared with a compressed tablet of 30 mg of fluorescein or fluorescein-dextran mixed with microcrystalline cellulose. In vitro dissolution tests performed in pH 7.4 phosphate buffer at 37°C showed that 50% dissolution of fluorescein from the patch preparation was more than two times slower than from the tablet preparation.

The three layered oral patch preparation was also evaluated in human volunteers using caffeine as a model drug. This preparation consisted of an ethyl cellulose backing layer, a layer of Eudragit L100 and a Carbopol based drug-carrying layer loaded with caffeine (50 mg). The three-layered preparation was heat-sealed, punched into patches 3 mm in diameter and administered in a batch of 120 by enteric encapsulation.

C) Microsphere patch
An alternative patch system similarly consists of three layers:
(i) A mucoadhesive layer
(ii) A layer of drug-loaded microspheres partially immersed in the mucoadhesive layer
(iii) An impermeable membrane encompassing the microspheres (Figure 6).

D) Insulin patch for oral delivery
A bilayered intestinal patch was designed for the oral delivery of insulin.44 These patches were fabricated using a mucoadhesive matrix of Carbopol, pectin and sodium CMC and loaded with bovine insulin (0.25–2.50 U/mg) as a model drug. The mixture was compressed under 0.5–4.0 tons using a hydraulic press and cut into disks with a diameter of 2–8 mm and a thickness of 400µm. Three sides of the patch were coated with a solution of ethylcellulose in acetone. The acetone was evaporated to obtain a 50µm thick ethyl-cellulose backing (Figure 7). The efficacy of the intestinal patch was evaluated in terms of insulin-induced hypoglycemia in rats, patch adhesion and insulin release.

E) Gated Hydrogels Patch
He et al. were able to assemble a drug delivery system that provides controlled release using

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.

1) 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.

2) Gamma Scintigraphy Technique

Distribution and retention time of the mucoadhesive tablets can be studied using the gamma scintigraphy technique. A study has reported the intensity and distribution of radioactivity in the genital tract after administration of technetium-labeled HAYAFF tablets. Dimensions of the stomach part of the rat can be outlined and imaged using labeled gellan gum, and the data collected are subsequently used to compare the distribution of radiolabeled HAYAFF formulations. The retention of mucoadhesive-radiolabeled tablets based on HAYFF polymer was found to be more for the dry powder formulation than for the press formulation after 12 h of administration to stomach epithelium. The combination of the sheep model and the gamma scintigraphy method has been proved to be an extremely useful tool for evaluating the distribution, spreading, and clearance of administered stomach mucoadhesive tablets.

CONCLUSION

There is no doubt that the oral route is the most favored and probably most complex route of drug delivery. Critical barriers such as mucus covering the GI epithelia, high turnover rate of mucus, variable range of pH, transit time with broad spectrum, absorption barrier, degradation during absorption, hepatic first pass metabolism, rapid luminal enzymatic degradation, longer time to achieve therapeutic blood levels, and intrasubject variability, are all possible issues with oral route. The idea of mucoadhesive began with the clear need to localize a drug at a certain site in the GI tract. Therefore a primary objective of the development of the mucoadhesive systems was achieved by obtaining a substantial increase in residence time of the drug for local drug effect and to permit once daily dosing. Several new patch systems have been developed to provide more effective oral drug delivery. These systems were designed to achieve the difficult task of performing multiple functions using a single platform, namely drug protection, unidirectional release and bioadhesion. In the near future, integrated smart device capable of fully autonomous delivery and site specific cell targeting will have a considerable impact on drug administration. A novel materials and technologies continue to emerge; the goal of manufacturing the ideal intelligent drug delivery device is rapidly being realized.

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1448-1453


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