1. Introduction

GASTRO-RESISTANT TABLETS

Gastro-resistant tablets are delayed-release tablets that are intended to resist the gastric fluid and to release their active substance(s) in the intestinal fluid. Usually they are prepared from granules or particles already covered with a gastro-resistant coating or in certain cases by covering tablets with a gastro-resistant coating (enteric-coated tablets).

Controlled drug delivery systems, which are intended to deliver drugs at predetermined rates for predefined periods of time, have been used to overcome the shortcomings of conventional drug formulations. Although, significant progress has been made in the controlled drug delivery area, more advances are yet to be made for treating many clinical disorders, such as diabetes and rhythmic heart disorders. In these cases, the drug has to be delivered in response to pH in the body. In fact, it would be most desirable if the drugs could be administered in a manner that precisely matches physiological needs at proper times (temporal modulation) and/or at the proper site (site-specific targeting). In addition, the controlled drug delivery area needs further development of techniques for delivery of peptide and protein drugs. In the body, the appearance of numerous bioactive peptides is tightly controlled to maintain a normal metabolic balance via a feedback system called ‘homeostasis’. It would be highly beneficial if the active agents were delivered by a system that sensed the signal caused by disease, judged the magnitude of signal and then acted to release the right amount of drug in response. Such a system would require coupling of the drug delivery rate with the physiological need by means of some feedback mechanism\(^1\).

The pH range of fluids in various segments of the gastrointestinal tract may provide environmental stimuli for responsive drug release. Studies by several research groups have been performed on polymers containing weakly acidic or basic groups in the polymeric backbone. The charge density of the polymers depends on pH and ionic composition of the outer solution (the solution into which the polymer is exposed). Altering the pH of the solution will cause swelling or deswelling of the polymer. Thus, drug release from devices made from these polymers will display release rates that are pH sensitive. Polyacidic polymers will be unswollen at low pH,
because the acidic groups will be protonated and hence unionized. With increasing pH, Polyacidic polymers will swell. The opposite holds for polybasic polymers, because the ionization of the basic groups will increase with decreasing pH. A practical consequence proposed is that these gels may not reliably mediate pH sensitive swelling controlled release in oral applications, because the levels of buffer acids in the stomach (where swelling and release are expected to occur) generally cannot be controlled. However, the gels may be useful as mediators of pH-triggered release when precise rate control is of secondary importance. This approach utilizes the existence of the pH gradient in the GIT that increases progressively from the stomach (pH 1.5-3.5) and small intestine (pH 5.5-6.8) to the colon (6.4-7.0). The most commonly used pH-sensitive polymers are derivatives of acrylic acid and cellulose. By combining the knowledge of polymers and their solubility at different pH environments, delivery systems have been designed to deliver drugs at the target site.

**GASTRO RETENTIVE TABLETS**

Tablet which remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs.

The gastroretentive drug 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.

Various parameters that need to be evaluated in gastro-retentive formulations include floating duration, dissolution profiles, specific gravity, content uniformity, hardness, and friability in case of solid dosage forms. In the case of multiparticulate drug delivery systems, differential scanning calorimetry (DSC), particle size analysis, flow properties, surface morphology, and mechanical properties are also performed.

Drug absorption from the gastrointestinal tract is a complex procedure and is subject to many variables. It is widely acknowledged that the extent of gastrointestinal tract drug absorption is related to contact time with the small intestinal mucosa. Gastroretentive systems
can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment.

Stomach Specific FDDS have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of fluctuations in plasma drug concentration. The floating sustained release dosage forms present most of the characteristics of hydrophilic matrices and are known as ‘hydrodynamically balanced systems’ (‘HBS’) since they are able to maintain their low apparent density, while the polymer hydrates and builds a gelled barrier at the outer surface. The drug is released progressively from the swollen matrix, as in the case of conventional hydrophilic matrices. These forms are expected to remain buoyant (3 on the gastric contents without affecting the intrinsic rate of emptying because their bulk density is lower than that of the gastric contents. Among the different hydrocolloids recommended for floating formulations, cellulose ether polymers are most popular, especially hydroxypropylmethylcellulose (HPMC). Fatty material with a bulk density lower than one may be added to the formulation to decrease the water intake rate and increase buoyancy.

**Mechanism of floating systems**

While the system is floating on the gastric the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been in the literature. The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to main submerged object. The object floats better if F is on the higher positive side. This apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseeable intragastric buoyancy capability variations.