STOMACH TARGETED MUCOADHESIVE DRUG DELIVERY FOR SELECTED 4-QUINOLONE ANTIBACTERIALS (OFLOXACIN) & ANTI-ULCER (RANITIDINE HYDROCHLORIDE)

1. INTRODUCTION

GASTRO-RETENTIVE DOSAGE FORMS (GRDF):

These are primarily controlled release drug delivery systems, which gets retained in the stomach for longer periods of time, thus helping in absorption of drug for the intended duration of time. Gastric retentive drug delivery devices can be useful for the spatial and temporal delivery of many drugs.

The gastric emptying time mainly depends upon on the design of the dosage form and physiological state of the subject, which last from a few minutes to 12hrs. The average gastric emptying time in human is 2-3hrs through major absorption zone (stomach and upper part of the intestine), which leads to incomplete drug release from the DDS leading to diminished efficacy of the administered dose. So drugs which have stability problem, GRDF plays an important role. These considerations have led to the development of oral controlled release dosage forms possessing gastric retention capabilities.

GRDF will also greatly improve the pharmacotherapy of the stomach itself through local drug release leading to high drug concentrations at the gastric mucosa, which are sustained over a long period of time.

Finally, GRDF will be used as carriers for drugs with so called absorption windows: these substances are taken up only from very specific sites of the gastrointestinal mucosa, often in a proximal region of the small intestine. Need of gastro retention arises because of two reasons.

- To improve bioavailability of drugs such as cyclosporin, ciprofloxacin, ranitidine, metoprolol tartarate etc. which are mainly absorbed from upper part of GIT or get degraded in alkaline pH.
- For local action in case of pathologies of stomach.
The stomach is a j-shaped organ located in the upper left hand portion of the abdomen just below the diaphragm. It occupies a portion of the epigastric and left hypochondriac 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.

**Gastric motility:**

Gastric emptying occurs during fasting as well as fed states. During the fasting state an interdigestive series of electrical events take place, which cycles through stomach and intestine every 2 to 3 hours. This is called the interdigestive myoelectric cycle or migrating myoelectric cycle (MMC), which is further divided into 4 phases as described below.

1. Phase I (basal phase) lasts from 40 to 60 minutes with rare contractions.
2. Phase II (preburst phase) lasts for 40 to 60 minutes with intermittent action and potential contractions. As the phase progresses the intensity and frequency also increases gradually.
3. Phase III (burst phase) lasts for 4 to 6 minutes. It includes intense and regular contractions for short period. It is due to this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the housekeeper wave.
4. Phase IV lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles.

After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state. This is also known as digestive motility pattern and comprises continuous contractions as in phase II of fasted state. These contractions result in reducing the size of food particles (to less than 1 mm), which are propelled toward the pylorus in a suspension form. During the fed state onset of MMC is delayed resulting in slowdown of gastric emptying rate. Scintigraphic studies determining gastric emptying rates revealed that orally administered controlled release dosage forms are subjected to basically two complication, that of short gastric residence time and unpredictable gastric emptying rate.
Gastrointestinal Transit Time:

Food content remains in each segment of the gastrointestinal tract for different periods of time. The resident time for both liquid and solid foods in each segment of the gastrointestinal tract is as reported by Park.

Bio/Muco-adhesive Systems

Bio/Muco-adhesive systems are those which bind to the gastric epithelial surface or mucin and serve as a potential means of extending the GRT of drug delivery system (DDS) in the stomach.

The surface epithelial adhesive properties of mucin have been well recognized and applied to the development of GRDS based on bio/muco-adhesive polymers. The ability to provide adhesion of a drug (or a delivery system) to the GI wall provides a longer residence time in a particular organ site, thereby producing an improved effect in terms of local action or systemic effect.

Binding of polymers to the mucin/epithelial surface can be divided into three broad categories:

1. Hydration-mediated adhesion.
2. Bonding-mediated adhesion.
3. Receptor-mediated adhesion.

1.1 Advantage

- Increasing the residence time of the drug formulation in the stomach and hence prolonging the period of contact with the mucosa, improve drug absorption. Approaches to increase the residence time of drug formulations in the stomach usually involve the use of tablets, microspheres, etc which have bioadhesive properties.
- The absorption and bioavailability will be increased due to prolong in the residence time.
• Can be utilized for all categories of the drugs which are stable in stomach and has less half life.

1.2 Limitations
The dosage forms should not burst in the stomach immediately, if it happens than whole drug will be washed out. Mucoadhesion is very essential.

1.3 Scope for the stomach targeted mucoadhesive drug delivery systems
• Future scope is high as we can deliver drug with reduced frequency which increases patient compliance.
• Dosing frequency will be reduced.
• Can be used for all categories of drugs, APIs, etc.