3 JUSTIFICATION & OBJECTIVE

3.1 Justification of the Project:

The most widely utilized and preferred route of administration amongst all the routes that have been explored till date is the oral route for the systemic delivery of drugs.

All the pharmaceutical products for systemic delivery via the oral route of administration, must be developed within the intrinsic characteristics of GI physiology, pharmacokinetics & pharmacodynamics and formulation design essential to achieve a systemic approach to the successful development of an oral pharmaceutical dosage form.1,2

The oral bioavailability can be affected by limited absorption site. The development of modified release product like once daily dosing becomes difficult and hence concept of absorption window has become popular.3,4 The Therapeutic window of many drugs is limited by their short circulating half life and absorption from a defined segment of the intestine. These limitations lead to frequent dosing to achieve the required therapeutic effect. This results in “pill burden” and consequently decreased patient compliance. The phenomenon of absorption via a limited part of GI tract has been termed as “narrow absorption window”, and once the dosage form passes the absorption window, the drug will neither be bio-available nor effective. In extreme cases, drugs that are insufficiently absorbed due to narrow absorption cannot be delivered entirely and are either given by a parenteral route or development of such medication which is otherwise safe and effective, is stopped altogether. A rational approach to enhance bioavailability and improve pharmacokinetic and pharmaco-dynamic profiles is to retain the drug reservoir above its absorption area, i.e. in the stomach and to release the drug in a controlled manner so as to achieve zero order kinetics (i.e. oral infusion) for a prolonged period of time.

The need for gastro retentive dosage forms (GRDDF) has led to extensive efforts in both academia and industry towards the development of such drug delivery systems.3,5
Another group of drugs that could benefit from retained and controlled release in the stomach are those meant for the treatment of pathologies located in the stomach, the duodenum or the small intestine.

Several approaches to extend the gastric retention time have been developed including an intra-gastric floating system, a high density system, a muco-adhesive system, a magnetic system and a super-porous hydro-gel system. An important issue in developing these systems is how to avoid inter-unit and inter-subject variations in GI residence times. Another problem is how to improve absorption of poorly absorbed drugs by using such systems. Drugs with narrow absorption windows in GI tract are particularly susceptible to variation in both bioavailability and time to achieve peak plasma levels. If successful, gastro retentive controlled release formulations could offer a potential solution to the problem by offering a prolonged gastric residence time.

Gastro-esophageal reflux disease i.e. GERD affects about 7% of the global population. In 1999 a review found that on an average 40% of GERD patients had Helicobacter pylori infection. Recent studies have shown an association between a long term infection with H. pylori and the development of stomach or gastric cancer. H. pylori has been recognized as a major gastric pathogen with worldwide distribution. H. pylori, a prevalent human specific pathogen is a causative agent in chronic active gastritis, gastric and duodenal ulcers and gastric adenocarcinoma, the second most common form of cancer in humans.

Mosapride citrate, a pro-kinetic agent which is indicated in the treatment of GERD, functional dyspepsia, diabetic gastro-pathy, etc., is an important drug in this therapy. In its conventional dosage it is required to be taken 3 to 4 times a day. It has a narrow absorption window and a short half life of 1.4 to 2 hrs. Thus it was an ideal candidate for GRDDF.

It is therefore necessary to design a drug delivery system that will not only alleviate the shortcomings of conventional delivery vehicles but also deliver the drug at a continuous predetermined rate to the site of action for a prolonged period of time.
3. Justification & Objective

The present study is undertaken for the development of gastro retentive technology which will deliver the drug at a predetermined rate to achieve the required concentration at the site of action for a prolonged period of time. This technology ensures the maximum utilization of the drug with minimum side effects, enhanced patient compliance, minimize drug accumulation due to chronic dosing and obtain less potentiation or deduction in drug activity with chronic use.

3.2 Objectives of the Project:

1. Development of gastro retentive floating controlled release dosage form of model drug Mosapride citrate based on factorial design.
2. To study the effect of polymer and binder on the floating behavior, physical parameters of the tablets and the drug release profile.
3. Evaluation of the drug loaded matrix for physical and chemical parameters.
4. Selection of the best formulation and validation of the formulation and process.
5. Study of mechanism and kinetics of release and their report.
6. In-vivo study of the finalized formulation for bioequivalence of the product.
REFERENCES


