3. RESEARCH ENVISAGED

3.1 Background

The development of oral transmucosal systems needs the extra study when in comparison with that of other conventional dosage forms. Bioadhesive tablets\textsuperscript{137} are kept in mouth release is been possible where oral mucosa absorbs directly where the drug are usually prepared by direct compression\textsuperscript{138}. Buccal patches have been prepared by solvent casting method and evaluated over the past several decades as a viable means of drug delivery to the tissues of the oral mucosa (i.e., buccal, palatal, and gingival tissues). Buccal adhesive patches\textsuperscript{139} are generally modified release dosage forms that have the potential to provide for controlled drug delivery from 1 to 24 h depending upon their biopharmaceutical and dissolution characteristics (i.e., slow dissolving Vs non-dissolving). A buccal patch refers broadly to a formulation framing a bioadhesive, that make the formulation that adhere to the oral mucosal tissue (i.e., buccal, palatal, and gingival, etc.) for varying periods of time (i.e., hours to days) to provide prolonged local or systemic drug delivery and these may be either slow dissolving or non dissolving tablets and patches. The FDA refers to these dosage routes and forms as buccal extended release films and tablets, respectively, but are defined more generically here as buccal patches. Buccal patch dosage forms are solid matrices that are generally non dissolvable or slowly dissolvable and can be designed to deliver the drug uni-directionally (i.e. directly into the
buccal tissue), bi-directionally (i.e. directly into the buccal tissue and into the saliva in the oral cavity), and multi-directionally (i.e. drug diffusion from all surfaces of the device).

### 3.2 Suitability of a drug

- Among H2 receptors Famotidine forms a competitive one, used as an anti-ulcerative agent. In the form of buccal films, buccal tablets and mucoadhesive hydrogels produces controlled delivery of the drug.
- Amount of drug available in Famotidine in oral doses is up to 40 to 45% so we can increases the bioavailability of drug through buccal film and buccal tablets.
- Plasma level is 1-3 h and it is having less first pass effect but in case of buccal film (or) buccal tablet the first-pass metabolism of drug have been avoided and the peak plasma level of drug occur in 12 h so therapy has to be maintained.
- By entrapment of drug in the form of buccal film (or) buccal tablet, the dose could be minimized.
- To improve the patient compliance.

By considering the above points the Famotidine might be a right and suitable candidate for the design of buccal films, buccal tablets and mucoadhesive hydrogels.
3.3 Aim and objective of work

The aim of present investigation is the development and evaluation of novel drug delivery system for H2 receptor antagonist of Famotidine with the following objectives

1. To prepare the buccal film, buccal tablets and mucoadhesive hydrogels of Famotidine with varying proportions of polymer.

2. To study the drug and polymer interaction.

3. To produce better bioavailability.

4. To minimize the dose.

5. To avoid presystemic elimination of the drug within the gastrointestinal tract.

6. A prolong period of time observed in oral cavity

7. Improve the patient compliance.
3.4 Plan of work

Lot of difficulties is involved in delivery of drugs via conventional routes. In the present study, the oral route, especially the buccal route and oral route was utilized as a platform for H2 receptor antagonist deliveries hence achieve of drug administration is minimal and on mucosa, site specificity is mainly achieved on reaching the systemic circulation. It shows a reduction in activity of enzymes in comparison with that of gastrointestinal, nasal region and a part of rectal administration. The work entitled “Development and evaluation of novel drug delivery system of selective H2 receptor antagonist” was planned in an aim to achieve the objectives the experimental work composed of four phases with like Pre-formulation studies, Formulation and evaluation of buccal films, buccal tablets and mucoadhesive hydrogels of Famotidine.

Phase I Pre-formulation studies

- Selection and collection of raw materials
- Drug-polymer compatibility studies by Physical observation
- Drug-polymer interaction studies by FTIR
- Drug-polymer interaction studies by DSC
- UV spectroscopic method development
- Construction of calibration curve
Phase II Formulation and evaluation of buccal films of Famotidine

- Fabrication of drug free buccal films.
- Fabrication of Famotidine buccal films
- Physicochemical evaluation of buccal films of Famotidine.
  - Thickness
  - Weight of films
  - Folding endurance
  - Surface pH
  - Percentage moisture absorption
  - Percentage moisture loss
  - Swelling percentage
  - Water vapor transmission rate
  - Drug content estimation
- Scanning electron microscopy
- Measurement of buccoadhesive strength
- Measurement of mechanical strength
- Drug release and kinetics studies
- Ex-vivo permeation studies through sheep buccal mucosa
- Ex-vivo muco irritation by histological examination
- In-vivo drug release studies on rabbits
- In-vivo drug release kinetics
- In-vitro In-vivo correlation
- Stability studies
Phase III Formulation and evaluation of buccal tablets of Famotidine

- Formulation of buccoadhesive tablets
- Physico-chemical evaluation of buccoadhesive tablets
  - Weight variation
  - Thickness
  - Friability
  - Hardness
  - Surface pH
  - Drug content
- Measurement of Buccoadhesive strength
- *In-vitro* swelling studies
- *In-vitro* drug release and kinetics studies
- *Ex-vivo* permeation study through sheep buccal mucosa
- *Ex-vivo* muco irritation by histological examination
- *In-vivo* drug release studies on rabbits
- *In-vivo* drug release kinetics
- *In-vitro In-vivo* correlation
- Stability studies
Phase IV Formulation and evaluation of mucoadhesive hydrogels of Famotidine

➢ Construction of calibration curve at pH 1.2 Hcl
➢ Formulation of mucoadhesive hydrogels
➢ Evaluation of Famotidine hydrogels
   ✓ Evaluation of micromeritic properties
   ✓ Evaluation of Equilibrium Swelling Ratio
   ✓ Water uptake studies
   ✓ Evaluation of gel fraction
   ✓ Morphological evaluation
   ✓ Physicochemical evaluation
➢ In-vitro test for mucoadhesion
➢ In-vitro drug release and kinetic studies
➢ Comparison of in-vitro drug release with marketed product
➢ In-vivo drug release studies on rabbits
➢ In-vitro In-vivo correlation
➢ Stability studies