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A Review on Mucoadhesive Tablets by Anti-Ulcer Drug Esomeprazole

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Abstract

Esomeprazole is a medication used in the treatment of gastroesophageal reflux disease (GERD), peptic ulcer disease, and Zollinger–Ellison syndrome. It is also used to prevent upper gastrointestinal bleeding in people who are at high risk. The Mucoadhesive buccal tablets were prepared by direct compression method using Chitosan, HPMC K100 and Carbopol p934 as mucoadhesive polymer. The compatibility studies of drug and excipients were performed by FT-IR spectroscopy. After examining the flow properties of the powder blends the results are found to be within prescribed limits and indicated good flowing property, hence it was subjected to tablet compression. The tablets were evaluated for post compression parameters like weight variation, hardness, thickness, friability, drug content uniformity, Surface pH, *in-vitro* studies like drug release. Formulation (F4) containing HPMC K100 in the ratio of (1:1) showed maximum drug release of 99.54% in 8 hrs. The drug content of shown highest of 99.61 %, Surface pH was found to be 6.05. All the evaluation parameters given the positive results and comply with the standards. The results indicate that the mucoadhesive buccal tablets of Esomeprazole may be good choice to bypass the extensive hepatic first pass metabolism with an improvement in the bioavailability of Esomeprazole through buccal mucosa.

Key words: Esomeprazole, Chitosan, HPMC K100, Carbopol p934and buccal tablets.

INTRODUCTION

Buccal delivery of drugs provides an attractive alternative to the oral route of drug administration, particularly in overcoming deficiencies associated with the latter mode of dosing.Problems such as first pass metabolism and drug degradation in the GIT environment can be circumvented by administering the drug via buccal route. Moreover, the oral cavity is easily accessible for self-medication and be promptly terminated in case of toxicity by removing the dosage form from buccal cavity. It is also possible to administer drugs to patients who cannot be dosed orally via this route Successful buccal drug delivery using buccal adhesive system requires at least three of the following (a) A bioadhesive to retain the system in the oral cavity and maximize the intimacy of contact with mucosa (b) A vehicle the release the drug at an appropriate rate under the conditions prevailing in the mouth and (c) Strategies for overcoming the low permeability of the oral mucosa. Buccal adhesive drug delivery stem promote the residence time and act as controlled release dosage forms.

The use of many hydrophilic macromolecular drugs as potential therapeutic agents is their in adequate and erratic oral absorption. However, therapeutic potential of these compounds lies in our ability to design and achieve effective and stable delivery systems. Based on our current understanding, it can be said that many drugs can not be delivered effectively through the conventional oral route.

The main reasons for the poor bio-availability of many drugs through conventional oral route are:

- ✓ Pre-systemic clearance of drugs.
- ✓ The sensitivity of drugs to the gastric acidic environment which leads to gastric irritation. Limitations associated with gastro intestinal tract like variable absorption characteristics.

Buccal mucosa composed of several layers of different cells. The Epithelium is similar to stratified squamous epithelia found in rest of the at least one of which is biological nature are held together by means of interfacial forces.[1]

Buccal drug delivery is a type of bioadhesive drug delivery especially it is a mucoadhesive drug delivery system is adhered to buccal mucosa.

- ➢ The term bioadhesion is commonly defined as an adhesion between two materials where at least one of the materials is of biological origin. In the case of bioadhesive drug delivery systems, bioadhesion often refers to the adhesion between the excipients of the formulation (i.e. the inactive media) and the biological tissue.
- ➢ The term mucoadhesion can be considered to refer to a sub group of bioadhesion and, more specifically, to the case when the formulation interacts with the mucous layer that covers a mucosal tissue.

The mucosal layer lines a number of regions of the body including gastrointestinal tract, urogenital tract, airway, ear, nose and eye. Hence mucoadhesive drug delivery system includes the following:

1. Buccal delivery system
2. Oral delivery system
3. Ocular delivery system
4. Vaginal delivery system
5. Rectal delivery system
6. Nasal delivery system[2]

Overview of the Oral Mucosa Structure The oral mucosa is composed of an outermost layer of stratified squamous epithelium. Below this lies a basement membrane, a lamina propria followed by the submucosa as the innermost layer18, 19 can be seen in figure 1. The epithelium of the buccal mucosa is about 40- 50 cell layers thick, while that of the sublingual epithelium contains somewhat fewer. The epithelial cells increase in size and become flatter as they travel from the basal layers to the superficial layers. The turnover time for the buccal epithelium has been estimated at 5-6 days[3], and this is probably representative of the oral mucosa as a

whole. The oral mucosal thickness varies depending on the site: the buccal mucosa measures at 500-800 μm, while the mucosal thickness of the hard and soft palates, the floor of the mouth, the ventral tongue, and the gingivae measure at about 100-200 μm. The composition of the epithelium also varies depending on the site in the oral cavity. The mucosae of areas subject to mechanical stress (the gingivae and hard palate) are keratinized similar to the epidermis. The mucosae of the soft palate, the sublingual, and the buccal regions, however, are not keratinized[4]. The keratinized epithelia contain neutral lipids like ceramides and acylceramides which have been associated with the barrier function. These epithelia are relatively impermeable to water. In contrast, nonkeratinized epithelia, such as the floor of the mouth and the buccal epithelia, do not contain acylceramides and only have small amounts of ceramide [5-7]. They also contain small amounts of neutral but polar lipids, mainly cholesterol sulfate and glucosyl ceramides. These epithelia have been found to be considerably more permeable to water than keratinized epithelia.

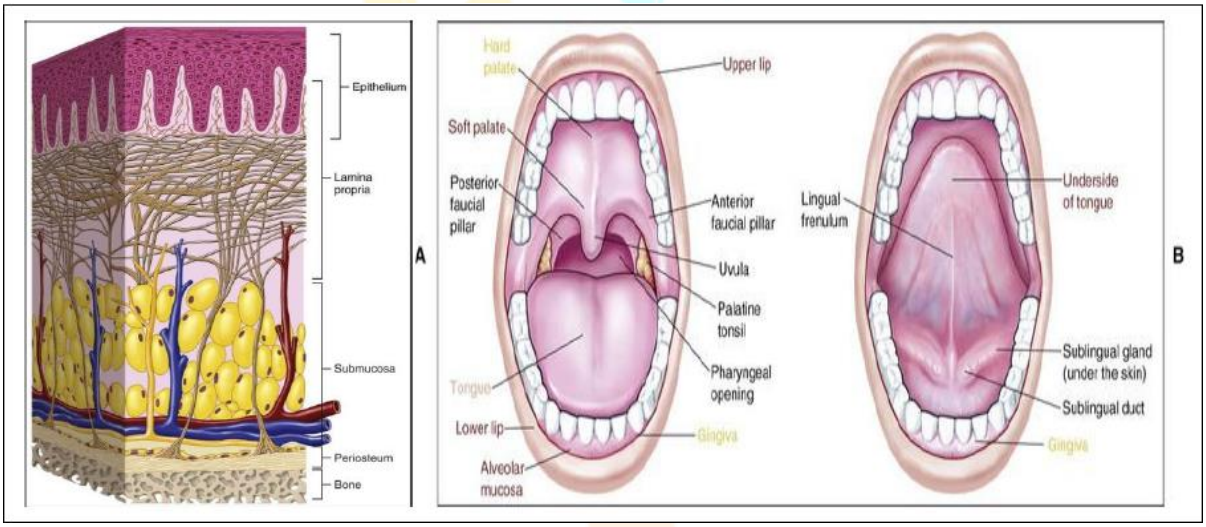

Figure 1.1: Anatomy of Oral Mucosa

Permeability

The oral mucosa in general is somewhat leaky epithelia intermediate between that of the epidermis and intestinal mucosa. It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of the skin[8]. As indicative by the wide range in this reported value, there are considerable differences in permeability between different regions of the oral cavity because of the diverse structures and functions of the different oral mucosae. In general, the permeabilities of the oral mucosae decrease in the order of sublingual greater than buccal, and buccal greater than palatal. This rank order is based on the relative thickness and degree of keratinization of these tissues, with the sublingual mucosa being relatively thin and non-keratinized, the buccal thicker and non-keratinized, and the palatal intermediate in thickness but keratinized.

Ideal Characteristics of Buccal Drug Delivery System [10]

- ✓ Should adhere to the site of attachment for a few hours.
- ✓ Should release the drug in a controlled fashion.
- ✓ Should provide drug release in a unidirectional way toward the mucosa.

- ✓ Should facilitate the rate and extent of drug absorption.
- ✓ Should not cause any irritation or inconvenience to the patient.
- ✓ Should not interfere with the normal functions such as talking and drinking.

ADVANTAGES

1) Bypass the gastrointestinal tract and hepatic portal system, increasing the bioavailability of orally administered drugs that otherwise undergo hepatic first-pass metabolism. In addition the drug is protected from degradation due to pH and digestive enzymes of the middle gastrointestinal tract.

2) Improved patient compliance due to the elimination of associated pain with injections; administration of drugs in unconscious or incapacitated patients; convenience of administration as compared to injections or oral medications.

3) Sustained drug delivery.

4) A relatively rapid onset of action can be achieved relative to the oral route, and the formulation can be removed if therapy is required to be discontinued.

5) Increased ease of drug administration.

DISADVANTAGES

1) Low permeability of the buccal membrane: specifically, when compared to the sublingual membrane.

2) Smaller surface area. The total surface area of membranes of the oral cavity available for drug absorption is 170 cm2 of which ~50 cm^2 represents non-keratinized tissues, including the buccal membrane.

3) The continuous secretion of saliva (0.5–2 l/day) leads to subsequent dilution of the drug.

4) Swallowing of saliva can also potentially lead to the loss of dissolved or suspended drug and, ultimately, the involuntary removal of the dosage form.

LIMITATIONS

1) Drugs which are unstable at buccal pH cannot be administered.

2) Eating and drinking may become restricted.

3) There is an ever-present possibility of the patient swallowing the dosage form.

4) Only drug with small dose requirement can be administered.

5) Only those drugs which are absorbed by passive diffusion can be administered by this route.

METHOD OF PREPARATION

Preparation of 0.2M Potassium Dihydrogen Orthophosphate Solution: Accurately weighed 27.218 gm of monobasic potassium dihydrogen orthophosphate was dissolved in 1000 mL of distilled water and mixed.

Preparation of 0.2M sodium hydroxide solution: Accurately weighed 8 gm of sodium hydroxide pellets were dissolved in 1000 mL of distilled water and mixed

Preparation of pH 6.8 phosphate buffer: Accurately measured 250 mL of 0.2M potassium dihydrogen ortho phosphate and 112.5 mL of 0.2M NaOH was taken into the 1000 mL volumetric flask. Volume was made up to 1000 mL with distilled water.

Preparation of pH 7.4 phosphate buffer: Accurately measured 250 mL of 0.2M potassium dihydrogen ortho phosphate and 195.5 mL of 0.2M NaOH was taken into the 1000 mL volumetric flask. Volume was made up to 1000 mL with distilled water.

Preparation of Tablets:

Then the powder blend was compressed into tablets by the direct compression method using 8mm flat faced punches. The tablets were compressed using a ten station LAB PRESS rotary tablet-punching machine. The weight of the tablets was determined using a digital balance and thickness with digital screw gauge.

MARKETED DRUGS

- Esomeprazole Gastro Resistant Tablets I.P.
- ESOMONT – 40 INJ, 40 mg
- Shelpraz D Capsules
- CortimentMmx 9mg Tablet PR
- 100 Mcg Plermin Gel
- Prucalopride Tablets 2mg
- Enalapril Maleate Tablets
- Carvedilol Tablets
- Candesartan Buccal Tablets
- Captopril Tablets
- Irbesartan Tablets

CONCLUSION

The present research was carried out to develop mucoadhesive buccal tablets of Esomeprazole using different types of polymers Chitosan, HPMC K100 and Carbopol p934. The preparation process was simple, reliable and inexpensive. All the prepared tablet formulations were found to be good without capping and chipping. The mucoadhesive buccal tablets of Esomeprazole could be prepared using Chitosan, HPMC K100 and

Carbopol p934 polymers by using direct compression method. The prepared mucoadhesive buccal tablets subjected to infrared spectrum study suggested that there was no drug -polymer interaction. It can be concluded that the formulation F4 will be useful for buccal administration for the treatment of gastroesophageal reflux disease (GERD), peptic ulcer disease, and Zollinger–Ellison syndrome. Hence the mucoadhesive buccal tablets of Esomeprazole may be a good choice to bypass the extensive hepatic first pass metabolism with an improvement in the bioavailability through buccal mucosa.

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