A

Project work on

“FORMULATION AND EVALUATION OF ESOMEPRAZOLE BUCCAL PATCHES”

by

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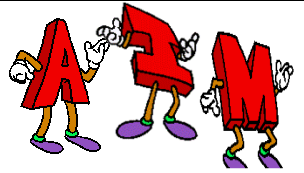


- Esomeprazole is class of drug called proton pump inhibitor used in the treatment of gastroesophagul reflux disease.

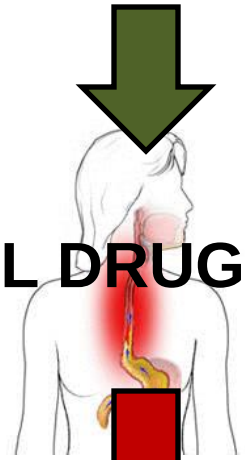
- It has a short half life 1 to 1.5 h and low oral bioavailability of 50%.

- Therefore, the purpose of this research was to develop unidirectional bucco-adhesive films of Esomeprazole by solvent casting technique.

- HPMC 50cps and Eudragit RL-100 were used as polymers in different proportion. Glycerol was used as plasticizer and Tween-80 was used as permeation enhancer.

INTRODUCTION

BUCCAL FILM / BUCCAL PATCH



BUCCAL DRUG DELIVERY

MUCOADHESIVE DRUG DELIVERY

MUCOADHESIVE DRUG DELIVERY SYSTEM

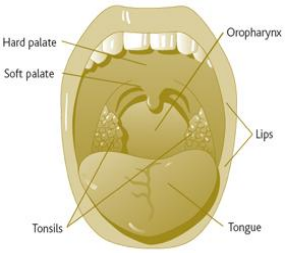
➢DEFINITION:

- It may be defined as a drug delivery system which utilize property of bioadhesion of certain water soluble polymers which become adhesive on hydration and hence can be used for targeting a drug to a particular region of the body for extended periods of time.

➢ADVANTAGES:

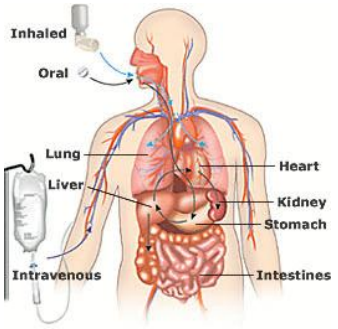
- First pass elimination associated with oral administration , so increase the bioavaibility and therapeutic activity.
- Both lipophilic and hydrophilic drug can be permeated.

TYPES OF MUCOADHESIVE DRUG DELIVERY SYSTEM

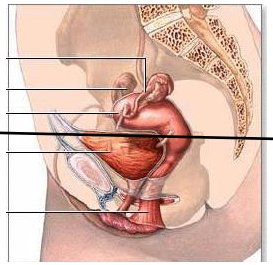


BUCCAL

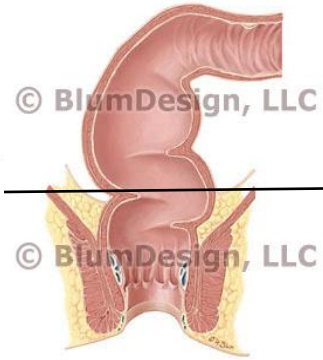
ORAL



VAGINAL



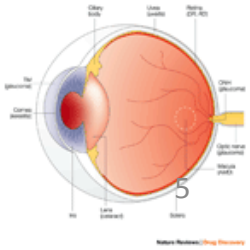
Mucoadhesive drug delivery System



RECTAL

NASAL

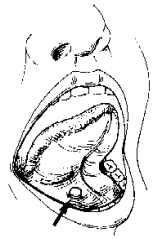
OCULAR



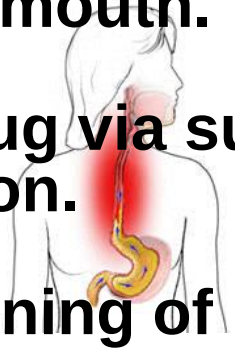
BUCCAL DRUG DELIVERY SYSTEM

Drug delivery according to membranes of oral cavity:

A. Sublingual delivery: The membrane of tongue and the floor of the mouth.



- **Administration of drug via sublingual mucosa to systemic circulation.**



B. Buccal delivery: The lining of cheeck.

- **Administration of drug via buccal mucosa to the systemic circulation.**

C. Local delivery: for the treatment of condition of the oral cavity.

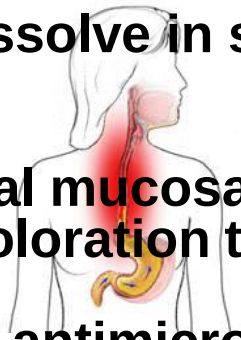
- **Eg. mouth ulcer, fungal condition.**

ADVANTAGES OF BUCCAL DRUG DELIVERY SYSTEMS

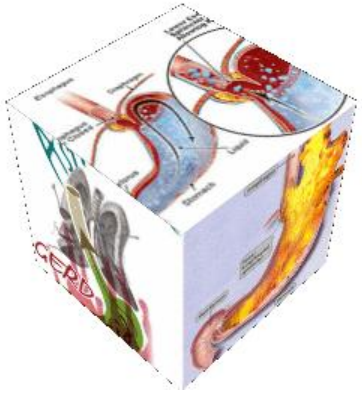
1. **Bypasses the hepatic first pass metabolism and greater bioavailability.**
2. **Delivery device can be made unidirectional.**
3. **Buccal mucosa is less prone to damage or irritation than oral mucosa.**
4. **Extent of perfusion is more , therefore quick and effective.**
5. **Nausea and vomiting are greatly avoided.**
6. **Used in case of unconscious and less co-operative patients.**
7. **Since the formulation is light:**
   - **Less transport cost**
   - **Economy of raw material**
   - **less packing cost**
   - **cheap**

DISADVANTAGES

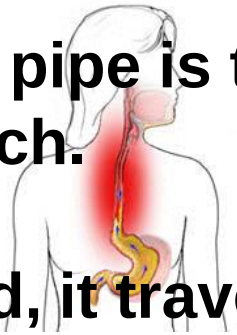
1. Relatively smaller area of absorption
2. The thickness of delivery system should be limited to a few millimeter in order to avoid inconveniences for patient.
3. Part of drug may be dissolve in saliva and may be swallowed.
4. Drugs which irritate oral mucosa or have bitter taste cause allergic reaction , discoloration teeth cannot be formulated.
5. If formulation contains antimicrobial agents, affect the natural microbial flora of mouth.
6. The patient cannot eat or drink or speak.
7. Only those drugs which are absorbed by passive diffusion can be administered by this route.
8. Drugs which are unstable at buccal pH cannot be administered by this route.



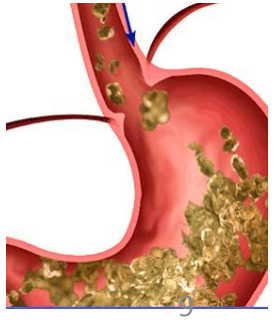
GERD



- Gastro esophageal reflux disease (GERD) is condition in which the esophagus becomes irritated or inflamed because of acid backing up from the stomach.



- The esophagus or food pipe is the tube stretching from the throat to the stomach.
- When food is swallowed, it travels down the esophagus.
- The stomach produces hydrochloric acid. When food enter into stomach the acid level in stomoch increase.



- So, acid travel in upward direction toward esophagus and which cause damage of esophagus.

For More Info on Life Style Changes & Treatment Options

www.AcidRefluxNYC.com

OBJECTIVE

1. To design and develop buccal patches of Esomeprazole.

2. To carry out preformulation studies for possible drug/polymer/excipients interactions by FTIR.

3. To formulate the drug delivery system using various excipients.

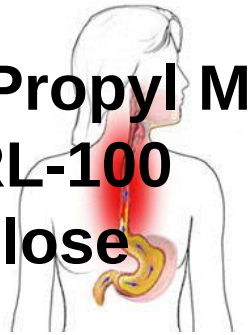
4. To evaluate the buccal patches using different parameter.

5. To carry out short term stability studies on the most satisfactory formulation as per ICH guidelines at 30 ± 2 ^{0}C (65 ± 5 %RH) and 40 ± 2 ^{0}C (75 ± 5 %RH).

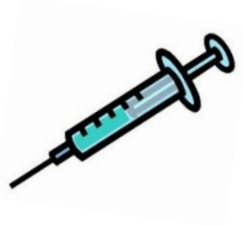
METHODOLOGY

MATERIALS:

- **Drug: Esomeprazole**

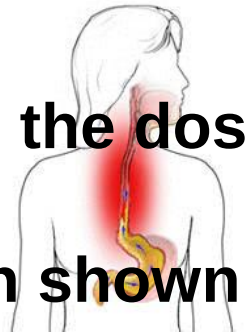


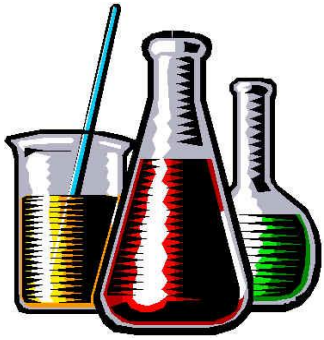
- **Polymers: Hydroxy Propyl Methyl Cellulose 50cps**
  Eudragit RL-100
  Ethyl cellulose
- **Plastcizer: Glycerol**
- **Penetration enhancer: Tween-80**
- **Solvent: Alcohol**



Dose selection

- For GERD, 20 or 40 mg of Esomeprazole is given once daily for 4-8 weeks.
- In children ages 1-11, the dose is 10 or 20 mg daily.
- 20 mg dose has been shown safe and effective in clinical studies.
- Therefore, 20 mg dose was selected for the designing of buccal drug delivery system in the present study.



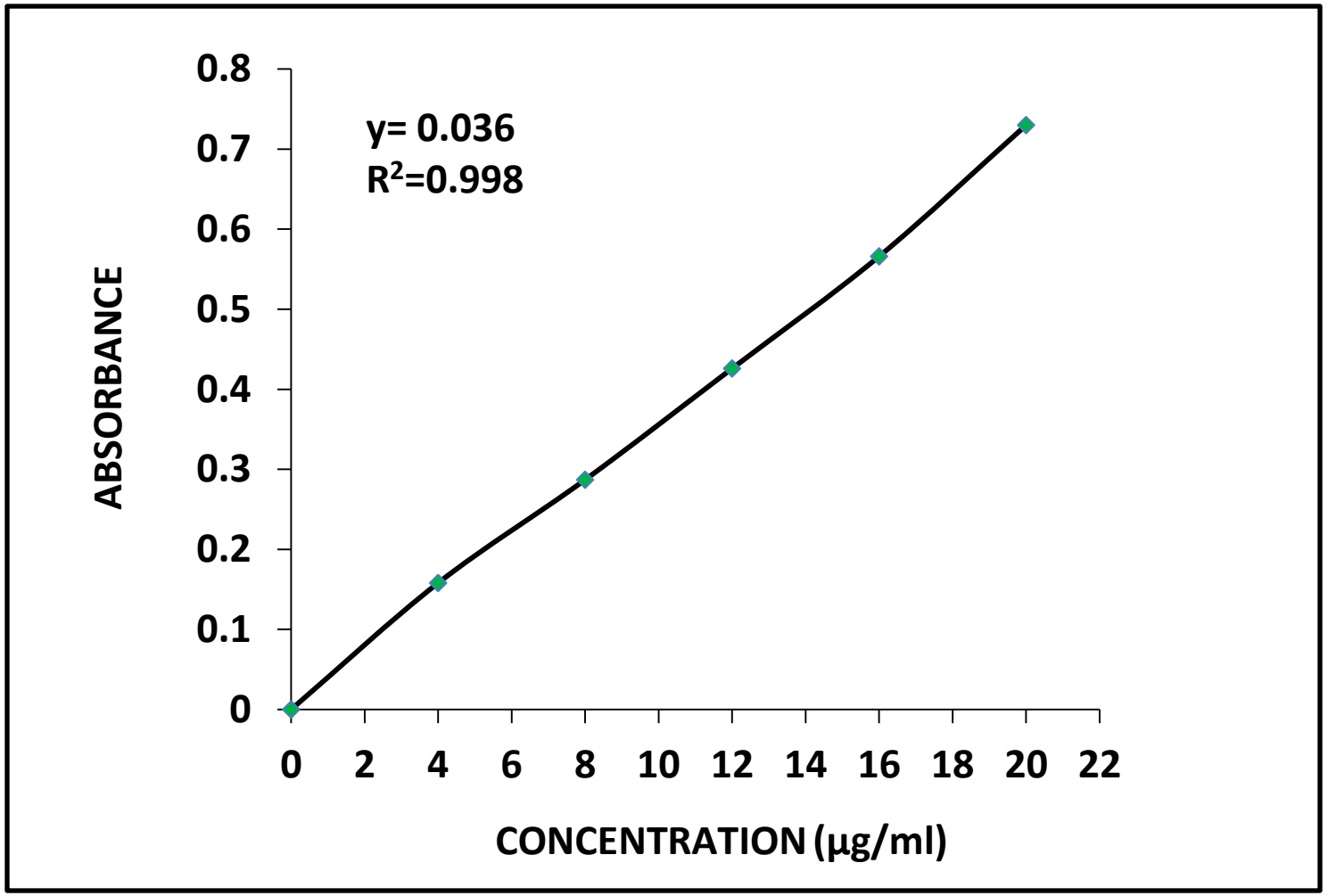


STANDARD CALIBRATION CURVE OF ESOMEPRAZOLE

- The standard solution of concentration 0, 4, 8, 12, 16 and 20 µg/ml of Esomeprazole were prepared in pH 6.8 phosphate buffer.

- The absorbance of these prepared solutions were measured at 302 nm using UV spectrophotometer.

UV Spectrum of Esomeprazole in simulated salivary fluid at pH 6.8

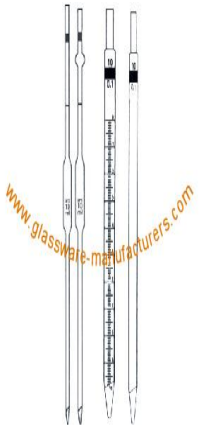


Procedure

- Buccal films were prepared by solvent casting technique.

- HPMC 50cps and Eudragit RL-100 were used in the preparation of films. Glycerol was used as a plasticizer. Tween-80 was used as permeation enhancer.

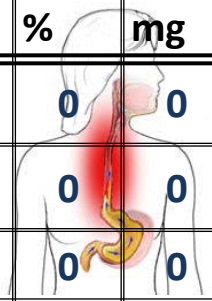
- The polymers were dissolved in solvent alcohol. The drug was then dispersed uniformly in the viscous solution ith continuous stirring.



- The resulting mass was poured into glass mould of 2.8 cm in diameter. The moulds were left undistu room temperature for one day. The films could b

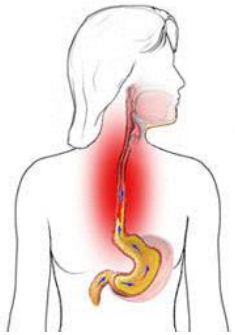
FORMULATION CHART

Formulation code	Amount of drug	Total Amount of polymer	Amount of HPMC 50cps		Amount of Eudragit RL-100		Amount of penetration Enhancer		Amount of plasticizer		Solvent
							Tween-80		Glycerol		
			In %	In mg	In %	In mg	In %	In ml	In %	In ml	In ml
F1	20	60	100	60	0	0	5	0.0037	20	0.012	5
F2	20	80	100	80	0	0	5	0.0046	20	0.015	6
F3	20	100	100	100	0	0	5	0.0050	20	0.019	7
F4	20	60	85	51	15	9	5	0.0037	20	0.012	5
F5	20	80	85	68	15	12	5	0.0046	20	0.015	6
F6	20	100	85	85	15	15	5	0.0050	20	0.019	7
F7	20	60	70	42	30	18	5	0.0037	20	0.012	5
F8	20	80	70	56	30	24	5	0.0046	20	0.015	6
F9	20	100	70	70	30	30	5	0.0050	20	0.019	7



EVALUATION OF ESOMEPRAZOLE BUCCAL PATCHES

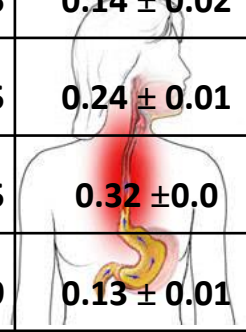
1. **Surface pH.**
2. **Swelling studies.**
3. **Weight uniformity.**
4. **Patch thickness.**



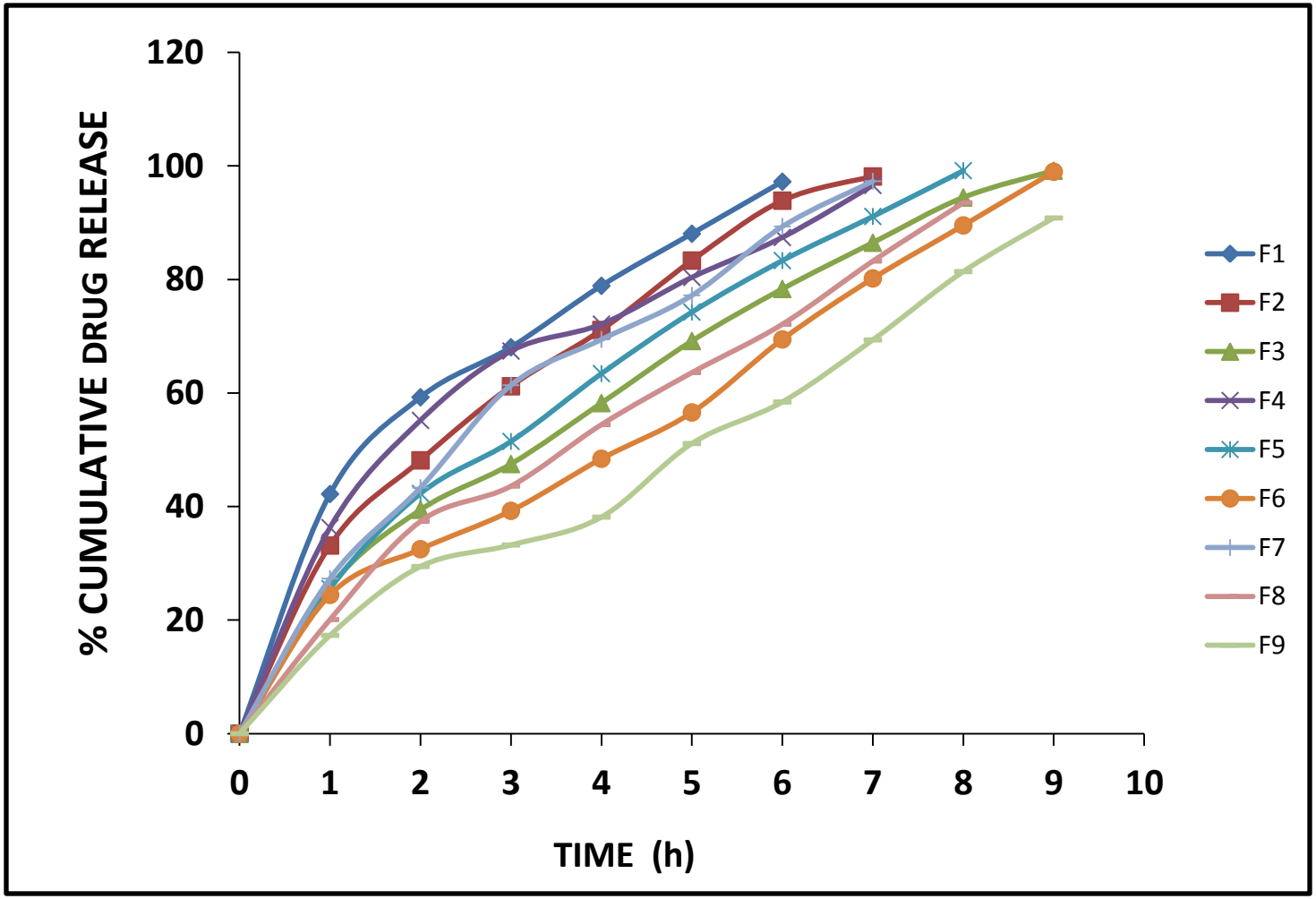
5. **Folding endurance of the patch.**
6. ***In-vitro* bioadhesive studies.**
7. ***In-vitro* release studies.**
8. ***Ex-vivo* permeation studies.**

PHYSICOCHEMICAL PARAMETERS OF VARIOUS FORMULATIONS

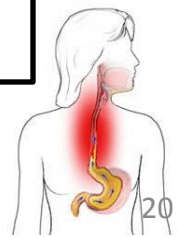
Formulation Code	*Surface pH*	*Swelling study	*Weight uniformity (mg)	*Thickness (mm)	*Folding endurance	*Drug content	*Bioadhesive strength
F1	6.20 ± 0.36	1.23	101.53 ± 1.85	0.14 ± 0.02	229.60 ± 2.50	99.14 ± 0.43	7.37 ± 0.04
F2	6.30 ± 0.30	1.31	125.13 ± 1.25	0.24 ± 0.01	251.00 ± 2.60	98.85 ± 0.65	9.23 ± 0.06
F3	6.23 ± 0.15	1.48	151.13 ± 2.45	0.32 ±0.0	268.00 ± 2.60	99.57 ± 0.43	11.40 ± 0.03
F4	6.56 ± 0.20	1.13	101.73 ± 2.69	0.13 ± 0.01	221.60 ± 2.50	98.85 ± 0.65	6.76 ± 0.06
F5	6.03 ± 0.25	1.22	124.93 ± 2.41	0.24 ± 0.02	247.60 ± 1.50	99.42 ± 0.24	8.25 ± 0.11
F6	6.36 ± 0.15	1.38	152.60 ± 1.80	0.34 ± 0.02	258.60 ± 2.80	98.73 ± 0.98	9.34 ± 0.05
F7	6.50 ± 0.20	1.07	102.08 ± 1.39	0.15 ± 0.01	215.00 ± 2.00	98.71 ± 1.13	5.91 ± 0.02
F8	6.16 ± 0.20	1.16	126.86 ± 2.30	0.24 ± 0.02	239.30 ± 1.50	98.42 ± 0.88	7.58 ± 0.01
F9	6.56 ± 0.25	1.24	150.93 ± 2.96	0.33 ± 0.02	251.00 ± 2.00	99.00 ± 0.65	8.63 ± 0.04

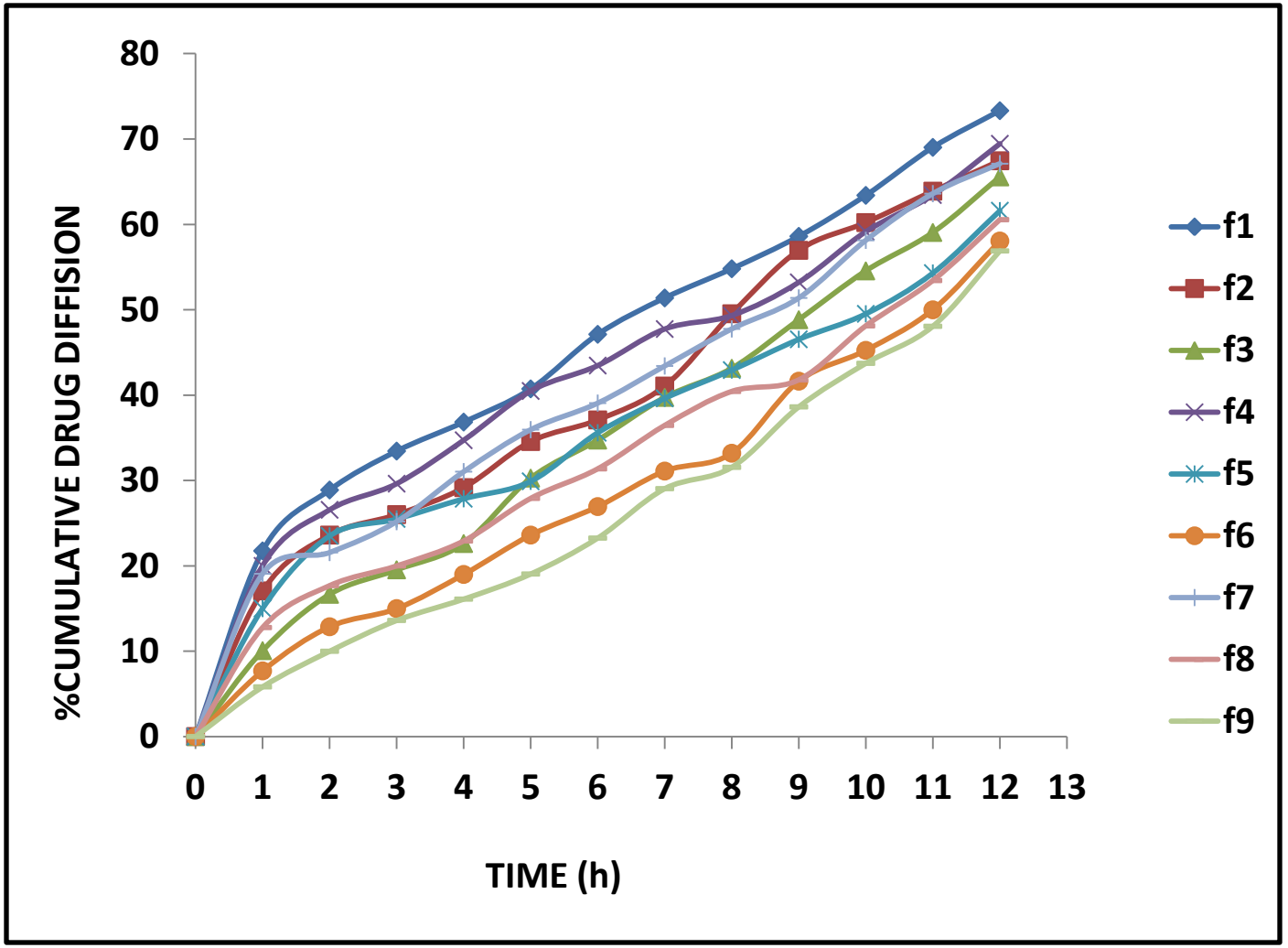


* Average value of three readings ± S.D

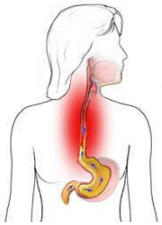


***[In-vitro* drug release studies of various formulations]**





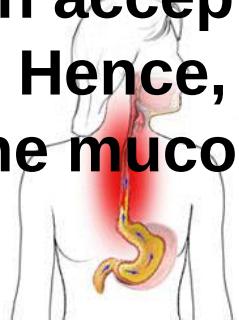
***[Ex-vivo* drug diffusion studies of various formulations]**



DISCUSSION

Surface pH:

- Surface pH of the formulation F1 to F9 varied from 6.03 ± 0.25 to 6.56 ± 0.25. Each sample was analyzed in triplicate (n=3). The results show that all the formulations provide an acceptable pH in the range of 5.5 to 7.0 (salivary pH). Hence, they will not produce any local irritation to the mucosa.



Swelling study:

- Swelling index of HPMC based formulations F1, F2 and F3 varied from 1.23 to 1.48%.
- Swellinindex of HPMC and Eudragit RL-100 based formulations F4, F5, F6, F7, F8 and F9 varied from 1.07 to 1.38%.

Folding Endurance :

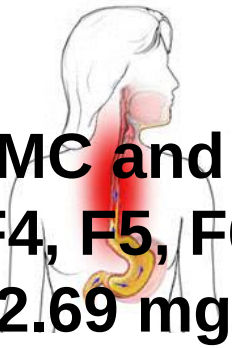
- Folding Endurance of the developed formulations F1 to F9 varied from 215 ± 2.0 to 268 ± 2.6 times which are within acceptable range.

Bioadhesion strength:

- Bioadhesion strength of HPMC based formulations F1, F2 and F3 varied from 7.37 ± 0.04 to 11.40 ± 0.03 g.
- Bioadhesion strength of HPMC and Eudragit RL-100 based formulations F4, F5, F6, F7, F8 and F9 varied from 5.91 ± 0.02 to 9.34 ± 0.05 g.
- As the amount of HPMC increases the *in-vitro* bioadhesion was found to be increased.
  So, formulation F3 showed greater bioadhesion strength (11.40 ± 0.03g).

Weight uniformity:

- Weight uniformity of HPMC based formulations F1, F2 and F3 varied from 101.53 ± 1.85 to 151.13 ± 2.85 mg.



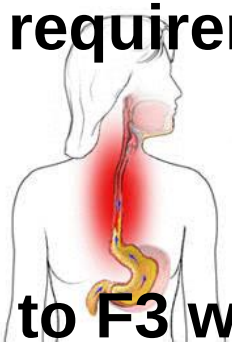
- Weight uniformity HPMC and Eudragit RL-100 based formulations F4, F5, F6, F7, F8 and F9 varied from 101.73 ± 2.69 mg to 152.60 ± 1.80 mg which is within acceptable range.

Thickness:

- Thickness of the developed formulations F1 to F9 varied from 0.13 ± 0.01 to 0.34 ± 0.02 mm which is within acceptable range.

Drug content:

- Drug content of the developed formulations F1 to F9 varied from 98.42 ± 0.88 to 99.57 ± 0.43% mg which was within the official requirements.



In-vitro release studies:

- In the formulations F1 to F3 which is having HPMC alone gives faster drug release as compared to other formulations which are having HPMC in combination with Eudragit RL-100 which retards drug release from the buccal films. Formulation F1 releases 97% drug within 6 h, while formulation F9 releases 90% drug within 9 h.

Ex-vivo Drug Diffusion Studies:

- **In the formulations F1 to F3 which is having HPMC alone gives more drug diffusion as compared to other formulations which are having HPMC in combination with Eudragit RL-100 which retards drug diffusion from the buccal films.**

- **Formulation F1 diffuses 73% drug within 12 h, while formulation F7 diffuses 67% drug within 12 h and formulation F9 diffuses 56% within 12 h.**

CONCLUSION

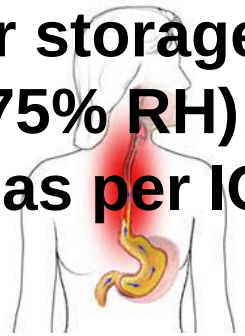
- Developed buccal films possessed the required physicochemical properties such as

Surface pH,
Swelling study,
Folding endurance,
Weight variation and
Bioadhesion strength.

The higher viscosity film forming polymers like Eudragit RL-100 had seemed to inhibit the initial burst release of Esomeprazole from the buccal films.

- From among all the developed formulations, since formulation F3 retarded the drug release for prolonged period of time (9 h) and diffused drug up to the 67.45%, it was selected as the best formulation.

- **The most satisfactory formulation had showed no significant change in physicochemical properties, drug content, bioadhesion properties, *in vitro* dissolution pattern or *ex-vivo* diffusion pattern after storage at 30ºC ±2 ºC (65% RH) and at 40 ±2 ºC (75% RH) during stability studies for 2 months as per ICH guidelines.**



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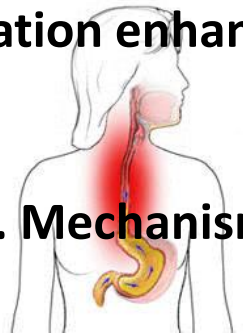

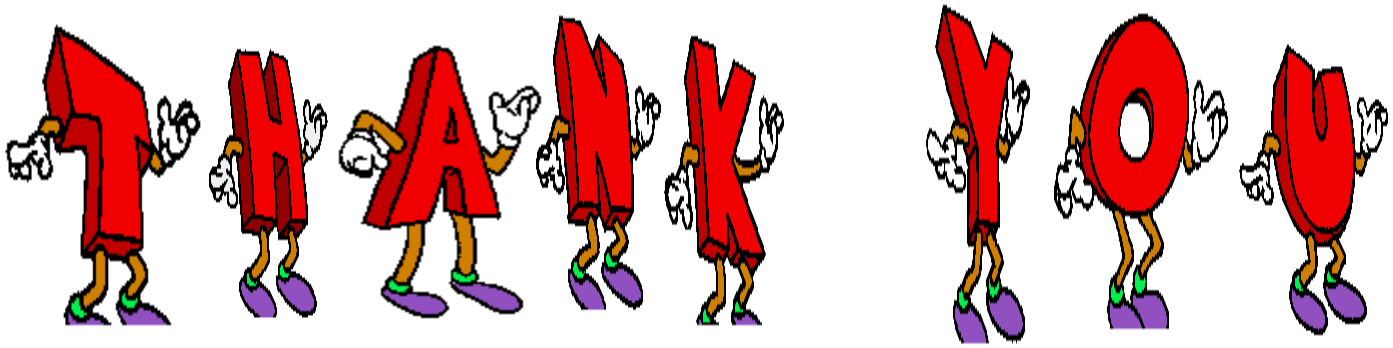
THANK YOU