CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.5746563

Available online at: http://www.iajps.com Research Article

FORMULATION, EVALUATION AND *IN-VITRO* CHARACTERIZATION OF ESOMEPRAZOLE LOADED FLOATING FILMS FOR GASTRIC DELIVERY

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Article Received: September 2021 **Accepted:** October 2021 **Published:** November 2021

Abstract:

Esomeprazole is a class of drug called proton pump inhibitors used in the treatment of Gastro Esophageal Reflux disease. Floating drug delivery system for Esomeprazole in the form of drug loaded films were developed and characterized for improving bioavailability. The films were formulated by solvent evaporation method using different polymers like HPMC K4M and Eudragit RL-100 by using plasticizers Poly ethylene glycol (PEG)-400. The physiochemical compatibility of the drug and the polymers was studied by FT-IR spectroscopy. The results suggested no physiochemical incompatibility between the drug and the polymers. The films were characterized on the basis of their physical characteristics like weight uniformity, thickness, folding endurance, dispersion test, drug content. By evaluation of formulated films, we can find best formulation on basis of bio adhesive studies.

Keyword: Esomeprazole, Drug loaded floating films, Solvent evaporation method.

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Please cite this article in press Shaffi Tangri and Dipankar Kurmi, ***Formulation, Evaluation And In-Vitro Characterization Of Esomeprazole Loaded Floating Films For Gastric Delivery.,*** *Indo Am. J. P. Sci, 2021; 08(11).*

INTRODUCTION:

Esomeprazole, the new S-isomer of omeprazole, is introduced to more effectively lower stomach acid output. When compared to omeprazole, esomeprazole has a much higher bioavailability, resulting in a larger suppression of stomach acid secretion.[1] The stereospecific S-isomer of omeprazole, Esomeprazole, was the first proton-pump inhibitor to be produced as a single isomer for the treatment of acid-related disorders.[2] The intragastric pH monitoring data for esomeprazole, 20 mg once daily, show an improvement over omeprazole, 20 mg once daily, but the intragastric pH monitoring data for esomeprazole, 40 mg once daily, show a more convincing gain in gastric pH management.[3] Early trails have revealed that esomeprazole has a similar tolerance and safety profile to omeprazole and achives higher and longer-lasting acid control. Furthermore, esomeprazole had a faster onset of acid suppression and less interindividual variance in acid control than omeprazole. Furthermore, a recent crossover research found that in individuals with symptomatic gastroesophageal reflux disease, esomeprazole at a standard dose of 40 mg once day provided more effective gastric acid control at steady state than conventional doses of pantoprazole, lansoprazole, and rabeprazole (GERD).[4] Furthermore, esomeprazole medication results in a higher percentage of erosive esophagitis healing and gives lasting heartburn relief in more patient than any other treatment.[5] GERD is a condition in which the stomach's digestive acid makes contact with the oesophagus (food ppe). Heartburn is the irritation induces by this condition. Long-term acid contact with the oesophagus can result in irreversible damage to the oesophagus.[6,7] Esomeprazole decreases the synthesis of digestive acids, reducing their esophageal irritation. In the 7-14 day eradiction triple therapy for helicobacter pylori, esomeprazole is coupled with the medicines clarithromycin and amoxicillin (or metronidazole in penicillin-hypersensitive patients). H. pylori infection is the cause of the majority of peptic and duodenal ulcers.

MATERIALS AND METHOD:

Esomeprazole was procured as gift sample from Torrent Pharmaceuticals, Selaqui, Uttrakhand. HPMC K4M, Eudragit RL 100, Polyethylene Glycol 400 (PEG), and Sodium Bicarbonate were commercially procured from Central Drug House Pvt. Ltd. All materials used in the formulation were of pharmacopoeial standards.

Preparation of Esomeprazole loaded floating films:

The esomeprazole film was prepared by using solvent evaporation method with various polymers HPMC K4M and Eudragit RL100. The amount of esomeprazole film was 20mg and appropriate amount of esomeprazole and sodium bicarbonate was dissolved in suitable amount of solvent ethanol and added to the polymer solution slowly with continuous stirring with magnetic stirrer, when drug polymer mixture mixed homogenously then added proper amount of plasticizer PEG 400 with continuous stirring. The obtained solution was drawn on the non-adhesive base plate and dried under infrared (IR) lamp for 24 h. After drying, the films were cut into suitable sizes.[8] Various trails were conducted to carried out optimize formula for the preparation of floating films. The various compositions of floating films are given in table no.1

Evaluation of Loaded films:

a) **Film Thickness:**
The film thickness was measured using screw gauge with a least count of 0.01 mm at different locations on the film. The film thickness was measured at three different locations, and the average weight was determined .

b) **Folding Endurance:**
Folding endurance is performed to determined the folding capacity of the film at extreme conditions. To determine folding endurance the films is folded at the same place until it break. The number of the times films folded without breaking is folding endurance value.

c) **Drug content:**
The content of drug uniformity of the films was tested by ultraviolet (UV)-visible spectrophotometric method. The absorbance values were determined at a wavelength of 300nm. The % drug content of various films was determined.

d) **Dispersion test:**
A film was placed in 200 ml of 6.8 pH phosphate buffer and was stirred for 3 min. Then, the resulting solution was passed through sieve number 22. The film passed the dispersion test only when no residue is left on the screen.

e) **Weight Uniformity:**
Randomly selection of 10 films and calculate their average weight. The individual weight of films dowst not deviate significant from the average weight.

***In vitro* dissolution study using Franz diffusion cell:**

It was determined using Franz diffusion cell with an constant volume of buffer (15ml) (Fig.2). The film equivalent to 20mg was placed in between the two compartments of an apparatus and pipette 15 ml of 6.8 pH buffer (pH of saliva) was added to receptor compartment. Cell is kept on magnetic stirrer and bead

in the cell is maintained at a speed of 50 revolution per minute (RPM), and medium was maintained at a temperature of nearly 32°C±0.5°C and withdraw 1ml of samples at various time intervals. The samples were diluted with 6.8pH phosphate buffer and measured the absorbance at 300 nm against 6.8 pH buffer as blank. [9,10] The various dissolution profiles for films are given in shown in Fig. 1.

Characterization:

Dissolution studies were performed on all the formulations and among this formulation, F4 was further evaluated by Fourier-Transform Infrared (FTIR) spectroscopy and differential scanning calorimetry.

FT-IR :

The FTIR spectra of esomeprazole, HPMC and Eudragit were obtained using Shimadzu- IR Affinity-FTIR Spectrophotometer to study the interaction between drug and carrier in films. The samples were prepared in KBr discs (2 mg sample in 200 mg KBr), and the sampling range was 400-4000 cm^{-1} and the resolution was 4 cm^{-1} . The FTIR spectra are shown in fig 2 and 3.

Table no. 1 : Formulation chart of floating films

Ingredients	E1	E2	E3	E4	E5
ESOMEPRAZOLE	20	20	20	20	20
HPMC K4M	200	400	200	400	200
EUDRAGIT RS100	50	100	50	100	100
PEG 400	0.3	0.7	0.7	0.3	0.7
SODIUM BICARBONATE	50	50	50	50	50
ETHANOL (ml)	10	10	10	10	10

Table no. 2 Evaluation of In-vitro dissolution parameters

Formulation	Thickness	Weight uniformity	Dispersion test	Folding endurance (%)	Drug content	Curling
F1	0.32	78	Passed	96	18.815	Absent
F2	0.34	91	Passed	92	18.557	Absent
F3	0.32	84	Passed	85	18.777	Absent
F4	0.34	102	Passed	105	19.995	Absent
F5	0.34	96	Passed	99	19.440	Absent

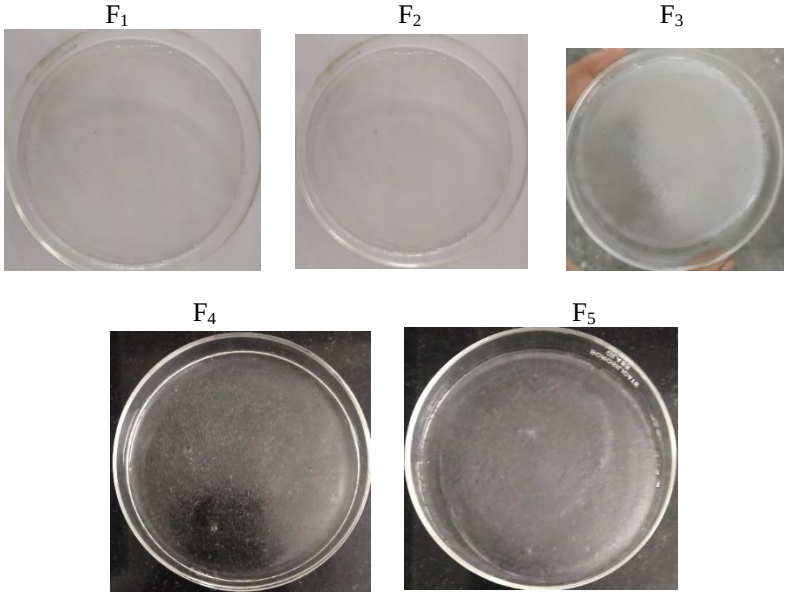
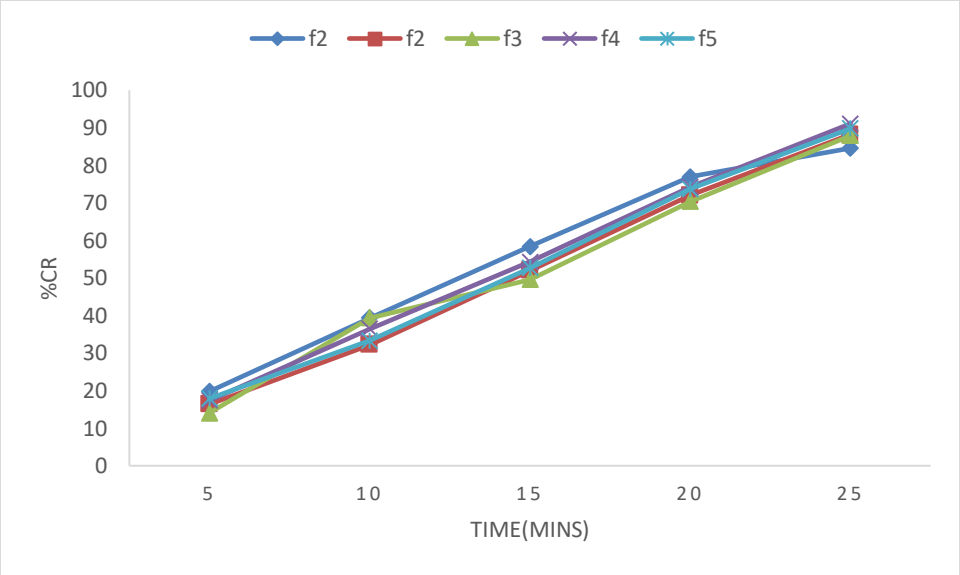


Fig 1. Esomeprazole loaded floating films



Fig, 2 Drug release profile of esomeprazole

RESULTS AND DISCUSSION:

Compatibility studies:

The present investigation deals with the formulation and evaluation of esomeprazole loaded floating films which is used for the treatment of acid-related disorders. The main focus on this study was to select the best combination of polymer and excipient to formulate acid related disorders floating films. Floating films were prepared by solvent evaporation method using HPMC K4M, Eudragit RL100, PEG 400, Sodium bicarbonate and ethanol. The composition of various floating films of acid related disorders is given in Table no. 1.

The prepared films were further evaluated for thickness, folding endurance, dispersion test, drug content and in vitro diffusion studies. The thickness of a film was found in the range of 0.032±0.001 – 0.034±0.004 mm. The optimized formulation E4 film is having thickness of 0.034 mm. The optimized formulation E4 film was found to have the folding endurance of 100% which is highly beneficial or agreeable. The drug uniformity was found in the range of 19.99±1.6 mg. The optimized formulation E4 film was found to have 19.99 mg. The film were further subjected to dispersion test as per the Indian Pharmacopeial standard.

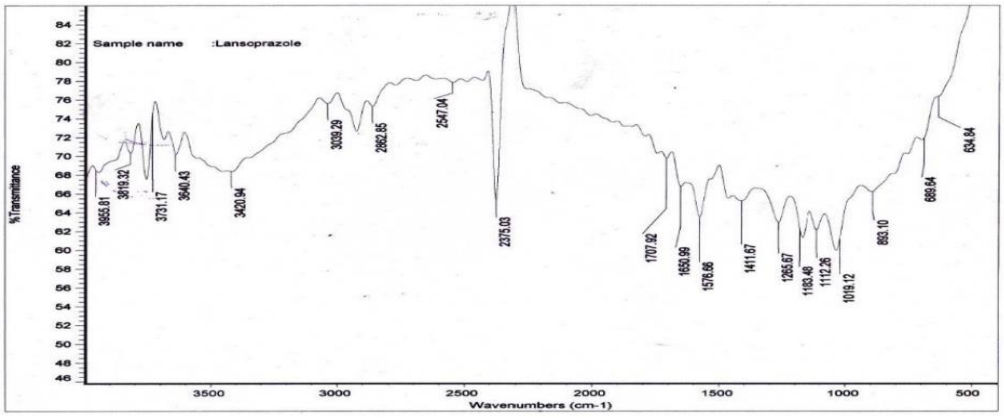


Figure no.1: FTIR of Esomeprazole

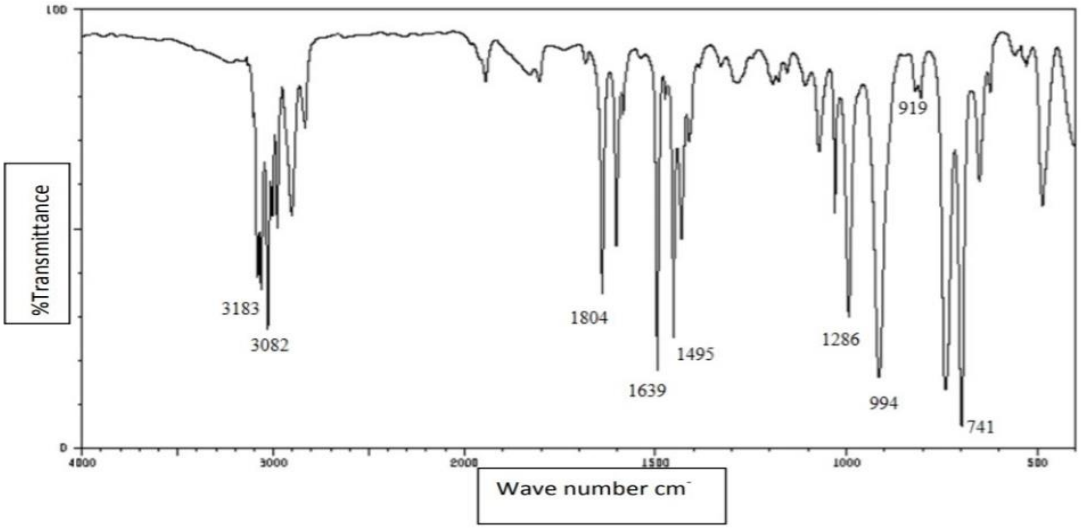


Figure no.2: FTIR of Esomeprazole + HPMC K4M

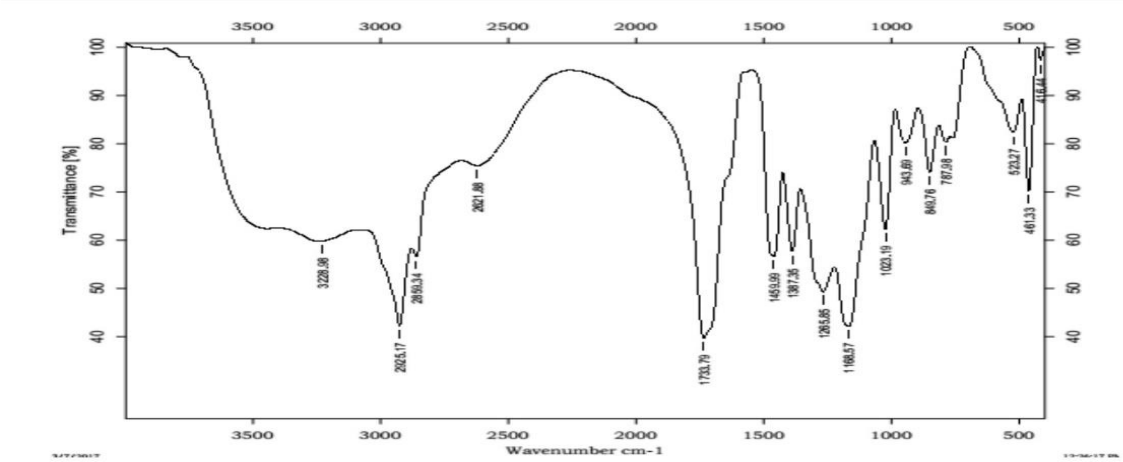


Figure no.3: FTIR of Esomeprazole + Eudragit

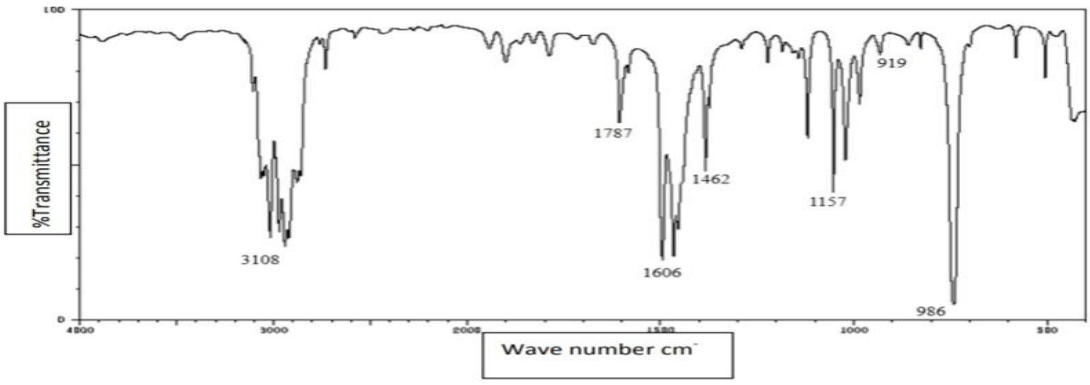


Figure no.4: FTIR of Esomeprazole + Sodium bicarbonate

Floating films of esomeprazole were further subjected to in-vitro dissolution studies Frantz diffusion cell with 15 mil of 6.8 pH phosphate buffer as a medium which is maintained at a temperature 32°c. The dissolution medium in the cell was maintained to rotate at 50 rpm using magnetic stirrer, The were withdrawn at various time intervals and were consequently diluted with 6.8 pH phosphate buffer, and absorbance values were noted at 300nm using Double beam spectrophotometer, Among all the formulations, formulation E4 was found to be best suitable for floating films also this film should possess all the physical characteristics required for the drug loaded floated film.The formulated films were characterized using FTIR. The FTIR spectra of the commercial sample of esomeprazole displayed bands at 3206 cm^{-1} due to N-H stretch and 2952 cm^{-1} due t C=C stretching. The IR spectra of drug and film forming agents indicated that there are no interactions between drug and excipients used.

CONCLUSION:

Esomeprazole loaded floating films prepared in the present study should exhibit good film properties as indicated by film thickness and folding endurance was measured. All the films prepared were found to be stable uniform, flexible, liable, and 91.12% of drug was released from optimized film E4 within 25 mins. Hence, floating films of esomeprazole were found to be suitable for effective and well-tolerated treatment option in the management of acid-related disorders.

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