

Formulation and evaluation of floating tablet of esomeprazole by using natural gums

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Abstract

Objective: The main objective of the study was to develop and evaluate the gastroretentive floating tablet of esomeprazole magnesium trihydrate, which is intended to increase patient compliance, deliver the medication in a controlled manner with less drug administration frequency, and increase the bioavailability of esomeprazole magnesium trihydrate.

Methods: In the current investigation, sodium bicarbonate was used as a gas-generating agent to create effervescent Esomeprazole magnesium trihydrate floating tablet formulations. Natural polymers like moringa gum, Azadirachta indica gum, sodium alginate, xanthan gum were used in the formulation of the tablets, which were made utilizing direct compression technology.

Results: All of the developed formulations showed good *In vitro* buoyancy. The tablets remained buoyant for 12 hours. The drug release profiles revealed that Moringa gum tablets had a more uniform and regulated release, releasing 96% of the drug. In comparison, neem gum tablets released 89% of the drug, xanthan gum tablets released 93%, and sodium alginate tablets released 96%.

Conclusion: Out of all the formulations developed, the F1 formulation had the highest *In vitro* dissolution results compared to the other batches, exhibiting the requisite sustained release time and acceptable floating qualities.

Keywords: Natural gum; Gastric residence time; Effervescent method; Buoyancy; Floating properties

1. Introduction

Floating or dynamically controlled systems are low-density systems that can stay afloat over stomach contents for a lengthy period of time without affecting gastric emptying rate. Mucoadhesion, flotation, sedimentation, expansion, as well as variable shape are some of the mechanisms that can be utilised to control stomach retention of solid dose forms. These methods indicate that floating drug delivery devices remain the most potential method of controlling medicine release [1]. To generate a tablet with the drug evenly distributed throughout the matrix, a blend powdered mixture consisting the therapeutic ingredient, a retardant component, and additional additives must be compacted directly. These systems continuously release the drug through mechanisms that are both diffusion as well as dissolution-controlled. [2,3].

Esomeprazole is a medicine that suppresses gastric acid output and is used to treat GERD, heal erosive esophagitis, and eliminate *H. pylori* to reduce the risk of repeated duodenal ulcer outbreaks. The second purpose is to assess the

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effectiveness of the co-processed excipients and compare how each influences the release of medication from different polymers. Esomeprazole, a BCS Class II drug (low solubility, high permeability), is used to treat acid reflux disease (GERD) [4,5]. Esomeprazole inhibits gastric acid secretion via specifically inhibiting H⁺/K⁺-ATPase in the gastric inferior cell. The S- and R-isomers of esomeprazole are protonated and transformed in the acidic compartment of the parietal cell, resulting in the active inhibitor, achiral sulphonamides [6]. By acting particularly on the Proton pump, a medication called prevents the final stage in acid generation, lowering stomach acidity [7,8].

In the past few years, there have been significant advances in various dosage forms for current and newly formulated pharmaceuticals and natural products, and semi-synthetic and synthetic excipients are frequently required for a number of applications. Gums and mucilage are often utilised natural materials for both traditional and new dosage forms. These natural materials have benefit over synthetic ones because they are chemically inert, non-toxic, less expensive, biodegradable, and widely available [9,10]. They can also be changed in many ways to produce tailored materials for drug delivery systems, allowing them to compete with synthetic excipients that are already available. Several polymers have been studied as drug retarding agents, each with distinct approaches to the matrix system [11]. Based on the characteristics of the delaying polymer, polymers that are hydrophilic are the best candidates for retarding drug release, and there is considerable interest in employing these polymers in sustained drug administration [12]. This review examines some of the most prominent plant-derived polymeric compounds utilised or studied as release retardants in sustained or controlled release medication delivery systems [13].

Moringa oleifera was tested as a binder and release retardant in tablet formulations. Moringa oleifera is a tiny, fast-growing tree found in India [14-15]. The tree's stem emits a white gum that turns reddish brown or brownish black with exposure [16]. Although slightly soluble in water, it produces a very viscous solution upon contact [17]. Collection and Cleansing of Neem Gum. Crude neem gum was recovered from the incised bark of *A. indica* trees on the local region of maharashtra. The recovered neem gum was hydrated in an adequate volume of distilled water for 5 days with periodic stirring, and extraneous elements were removed by filtering through a Buchner funnel at negative pressure [18,19]. The gum from the filtered mixture was precipitated with 99.8% ethanol, filtered, washed multiple times with acetone, and dried in a hot air oven at 30°C for 96 hours before grinding and sieving with a mesh no. 60 (250 µm). It was then stored in an amber-colored bottle until used [20].

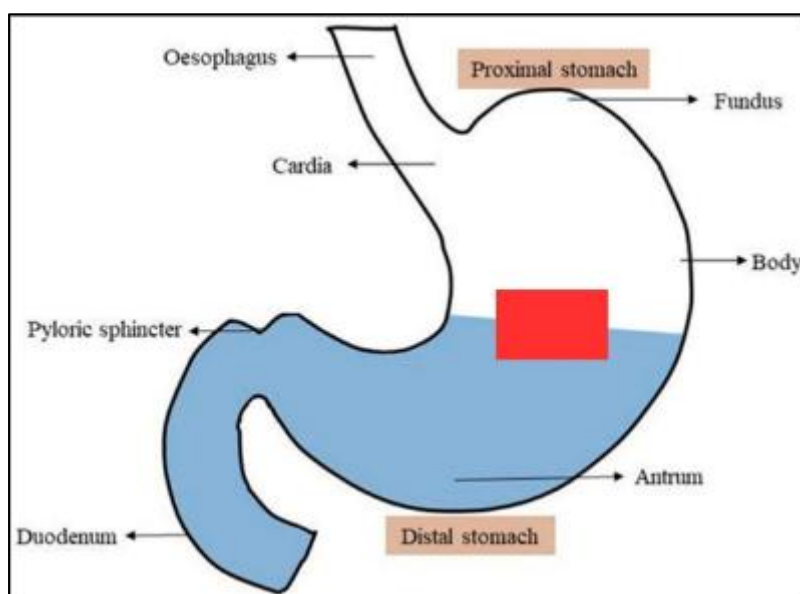


Figure 1 Floating drug delivery system

1.1. Advantages of FDDS

- For medications that are absorbed through the stomach, such as antacids and ferrous salts, the gastroretentive systems are beneficial.
- Drugs intended for local action in the stomach benefit from the gastro retentive systems such as antacids.

- Poor absorption is anticipated when there is a strong bowel movement and a brief transit period, as may be the case with some types of diarrhoea. In certain situations, it might be advantageous to keep the medication floating in the stomach in order to obtain a comparatively better reaction [21].
- FDDS reduces dosage frequency, which enhances patient compliance.
- Drugs with a short half-life may have better therapeutic effects.
- The duration of gastric retention is longer due to buoyancy.
- Better absorption of medications that only dissolve in the stomach.
- Due to the avoidance of fluctuations in plasma drug concentration, bioavailability improves the first pass effect; a desirable plasma drug the medication is released continuously to sustain concentration [22]

1.2. Disadvantages of FDDS

- Gastric retention is influenced by a variety of factors such as gastric motility, pH, and the presence of food, all of which are variable. So, buoyancy cannot be predicted.
- The medications which cause irritation to the gastrointestinal mucosa, having solubility and stability difficulty are not suited for manufacturing the floating drug delivery system.

2. Materials and methods

Table 1 List of Material

Sr. No.	Materials	Supplied by
1	Esomeprazole magnesium trihydrate	Smart Laboratories Pvt. Ltd. (Gift sample)
2	Xanthan Gum	Yucca Enterprises Mumbai
3	PVP K 30	Research Lab Fine Chem Industries Mumbai
4	Carbopol 120	Research Lab Fine Chem Industries Mumbai
5	Sodium bicarbonate	Research Lab Fine Chem Industries Mumbai
6	Magnesium stearate	Research Lab Fine Chem Industries Mumbai
7	Talc/ Talcum powder	Chemdyes Corporation Gujarat
8	Sodium alginate	Research Lab Fine Chem Industries Mumbai
9	Azadirachta indica gum	Obtained from bark of the plant Azadirachta indica
10	Moringa gum	Obtained from bark of the plant Moringa oleifera Lam.

2.1. Pre-formulation Study

2.1.1. Analytical Method: Estimation of Esomeprazole Magnesium Trihydrate

Preparation of calibration curve

Standard stock solution of Esomeprazole was prepared by dissolving 10mg of Esomeprazole in 10 ml of Methanol and distilled water (50:50) which gives 1000 μ g/ml. One ml of this stock solution was taken and was diluted up to 10ml by using methanol and distilled water (50:50) to produce a concentration of 100 μ g/ml Solution. From the above stock make concentration like 2,4,6,8,10,12,15 μ g/ml according to beers lambert law and all solution analyse on UV Spectrophotometer. Then taking the absorbance, calibration curve was plotted taking concentration on x-axis and absorbance on y-axis which showed a straight-line linearity shown by value of r^2 .

2.1.2. FT-IR Study

The FT-IR analysis of the Esomeprazole magnesium was carried out for qualitative compound identification. The FT-IR spectra for pure drug and with other excipients was obtained by placing the drug directly into the cavity and was determined by FT-IR spectrophotometer in the wave number region of 4000-400 cm^{-1} [23].

2.1.3. Pre-compression parameters

Bulk Density

The bulk density of a material is defined as its mass (weight) to volume ratio. A powder's bulk density is determined by its particle size distribution. The bulk density can be found using the following equation:

$$\text{Bulk density} = \text{weight of powder} / \text{initial volume}$$

Tapped Density

A graduated cylinder with a known mass of medication is placed on a mechanical tapper equipment, which is operated for a defined number of taps (about 1000) until the minimum powder bed volume is attained. This process determines the tapped density. The drug weight in the cylinder and the tapped volume are used to calculate the tapped density [24].

$$\text{Tapped density} = \text{weight of powder} / \text{Tapped volume}$$

Angle of Repose

The greatest angle that can exist between the surface of a powder pile and a horizontal plane is known as the angle of repose. The funnel method was used to calculate the angle of repose. A 2.5-centimeter-tall funnel with a 10-millimeter inner stem diameter was placed above the platform. A sample weighing about 10 grams was gradually moved along the funnel's wall until the pile's tip formed and came into contact with the funnel's stem. The powder was let to freely pour onto the surface through the funnel. It was measured how big the powder cone was. The radius of the powder cone was estimated to be nine and a rough circle was drawn around the base of the pile [25]. computed using the formula that follows:

$$\text{Tan } \theta = H/R$$

Where, θ = angle of repose,

h = height of the pile,

r = average radius of the powder conc.

Compressibility Index:

Carr's compressibility index 10 was used to get the granules' compressibility index [26].

$$\text{Carr's Index} = [(\text{tapped density}) - (\text{bulk density}) / (\text{tapped density})] \times 10$$

Hausner's Ratio:

A measure of a powder's flowability is the Hausner's ratio. The given equation is used to compute Hausner's ratio.

$$\text{Hausner's ratio} = \text{Tapped density} / \text{Bulk density.}$$

Table 2 Specifications of flowability for car's index Hausner's ratio

Flow character	Carr's index (%)	Hausner's ratio
Excellent	≤ 10	1.00-1.11
Good	11-15	1.12-1.18
Fair	16-20	1.19-1.25
Passable	21-25	1.26-1.34
Poor	26-31	1.35-1.45
Very poor	32-37	1.46-1.59
Very very poor	>38	>1.60

2.2. Preparation of Esomeprazole Magnesium Trihydrate floating tablet

Floating tablets of Esomeprazole were prepared by direct compression method using different Ingredient.

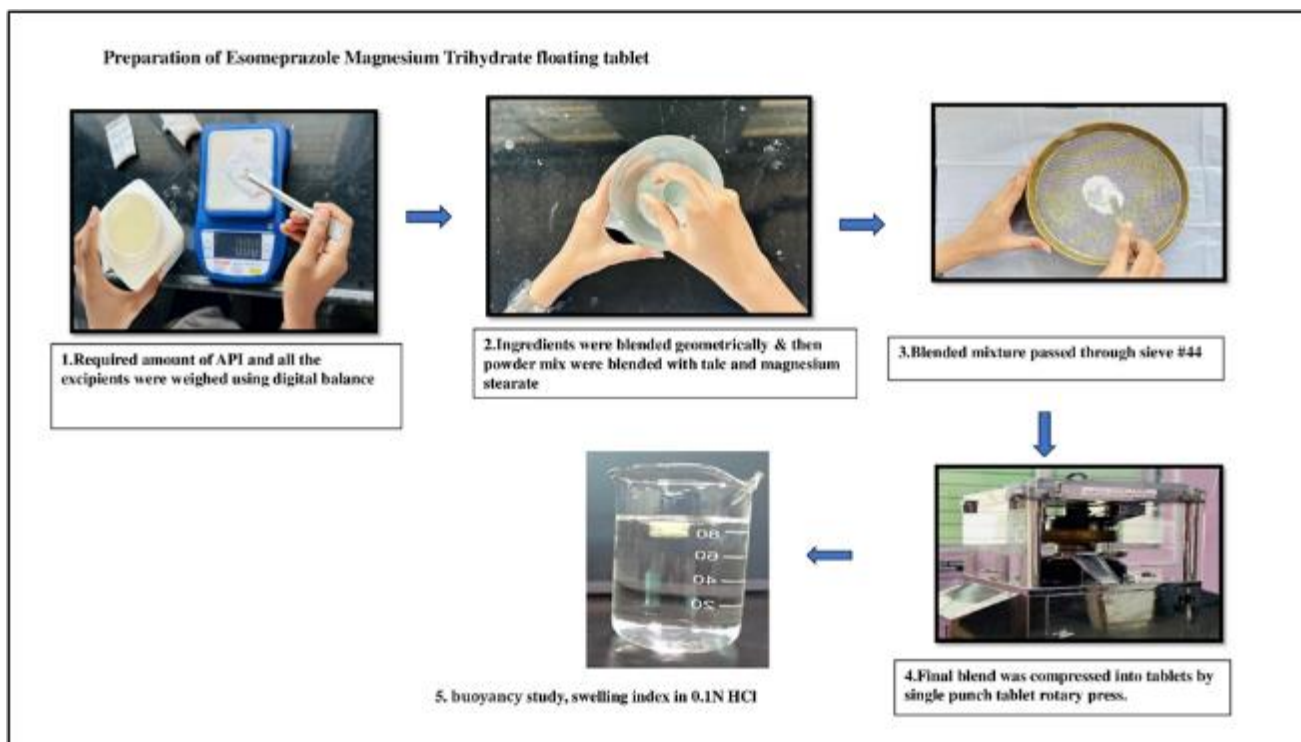


Figure 2 Practical representation of Preparation of Esomeprazole floating tablet

Table 3 Formulation table

Ingredients	F1	F2	F3	F4
Drug	40	40	40	40
Moringa gum	100	-	-	-
Azadirachta indica gum	-	100	-	-
Sodium Alginate	-	-	100	-
Xanthan gum	-	-	-	100
Sodium bicarbonate	80	80	80	80
PVP K 30	40	40	40	40
Carbopol	130	130	130	130
Magnesium stearate	5	5	5	5
Talc	5	5	5	5
Total (mg)	400	400	400	400



Figure 3 Performed formulated batches F1-F4

2.3. Evaluation of Post-Compression Parameters

2.3.1. General Appearance

The first and most crucial factor influencing a tablet's adoption is its organoleptic qualities, or overall appearance. Its significance for consumer approval cannot be overstated. The organoleptic qualities of the prepared tablets (colour, odour, taste, and form) were assessed.

2.3.2. Thickness

Six tablets, one for each formulation, were chosen at random, and the thickness was measured using a vernier calliper before the average value was determined [27].

2.3.3. Friability

The friability was calculated using the Roche friabilator, and the result is given as a percentage. Twenty pills were taken, weighed at first (W_{initial}). The friabilator was filled with preweighed tablets and set to spin for four minutes at 25 rpm (100 revolutions per minute). Subsequently, the tablets were taken out of the chamber, cleaned, and weighed one more (W_{final}) [28,29]. Next, the percentage friability was determined by:

$$F = \frac{[(W_{\text{initial}}) - (W_{\text{final}})]}{(W_{\text{initial}})} \times 100$$

2.3.4. Hardness

The term "hardness of tablet" describes a tablet's resistance to mechanical shocks. Tablet breaking points are tested via hardness testing. Six pills of each formulation were used. The Monsanto hardness tester was used to measure the tablet's hardness. The unit of hardness was kg/cm^2 [30]

2.3.5. Weight Variation

From each formulation, 20 tablets were selected at random and weighed separately. Using the provided formula, the average weight was computed, and the % departure from the average weight was found.

$$\% \text{ deviation} = \frac{[(\text{Average weight} - \text{initial weight}) / \text{Average weight}] \times 100}$$

2.4. *In vitro* buoyancy/Floating study

Studies on buoyancy *In vitro* were conducted on each formulation. Each formulation's randomly chosen tablets were stored in a 100 ml beaker filled with 0.1N HCL pH 1.2. The floating lag time was the amount of time it took for the tablet to rise to the surface and float, and the total floating time (TFT) was the amount of time the dosage form stayed on the medium's surface continuously [31-33].

2.4.1. Swelling Studies

The tablets that were ready were put into a glass that had 200 ml of 0.1 N HCl at $37 \pm 0.5^\circ\text{C}$. Using the following equation, the proportion of swelling at various time intervals was determined [34].

$$SI (\%) = W2 - W1 / W1$$

Where,

W1= Initial weight of tablet,

W2= Weight of tablet after time interval t.

2.5. *In-Vitro* Dissolution Studies

Esomeprazole floating tablet *In vitro* dissolving investigations were conducted utilizing USP type II apparatus (paddle type). After adding 900 ml of 0.1 N HCL pH 1.2 to the dissolution vessel, the medium's temperature was raised to $37 \pm 0.50^\circ\text{C}$. After setting the paddle's rotational speed to 50 revolutions per minute, one pill was added to each dissolving vessel [35,36]. During eight hours, 10 ml of solution were taken out of the dissolving containers every hour, and 10 ml of new dissolution media were added to the samples. This solution's absorbance was determined at 218 nm using a UV spectrophotometer.

3. Result and discussion

3.1. Calibration curve

The medication Esomeprazole has a λ max of 301 nm in its UV spectrum. Table 5 and Figure 8 display the data for the Esomeprazole calibration curve. With a r^2 of 0.9932, a slope of 0.0775, an intercept of 0.048, and a concentration range of 2, 4, 6, 8, 10, 12, 15 ($\mu\text{g}/\text{ml}$) the calibration curve was built by using UV Spectrophotometer.

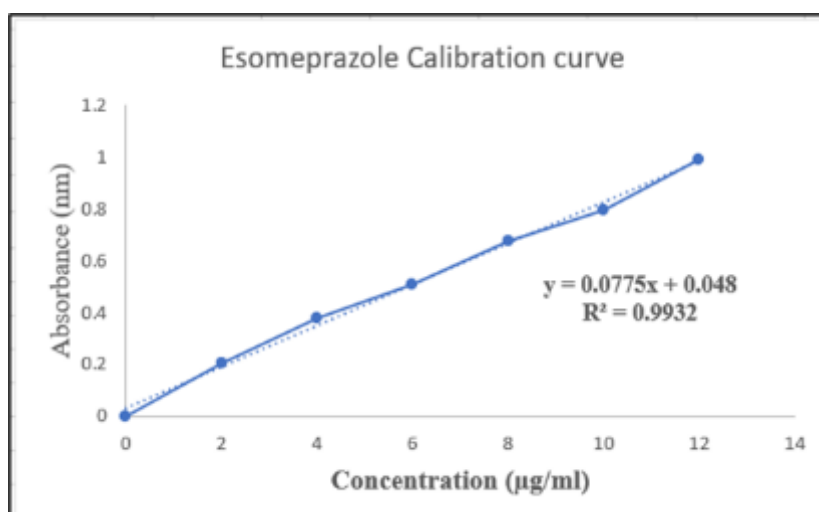


Figure 4 Esomeprazole-Calibration Curve

3.2. FTIR Study

Compatibility studies were carried out using FTIR spectroscopy to identify potential interactions between the excipients used in the formulation, the medicine Esomeprazole, and Moringa gum gum. When comparing the wave numbers to the values of the pure drug, there was no discernible change in position. Consequently, there was no interaction between the medication and the formulation's other excipients.

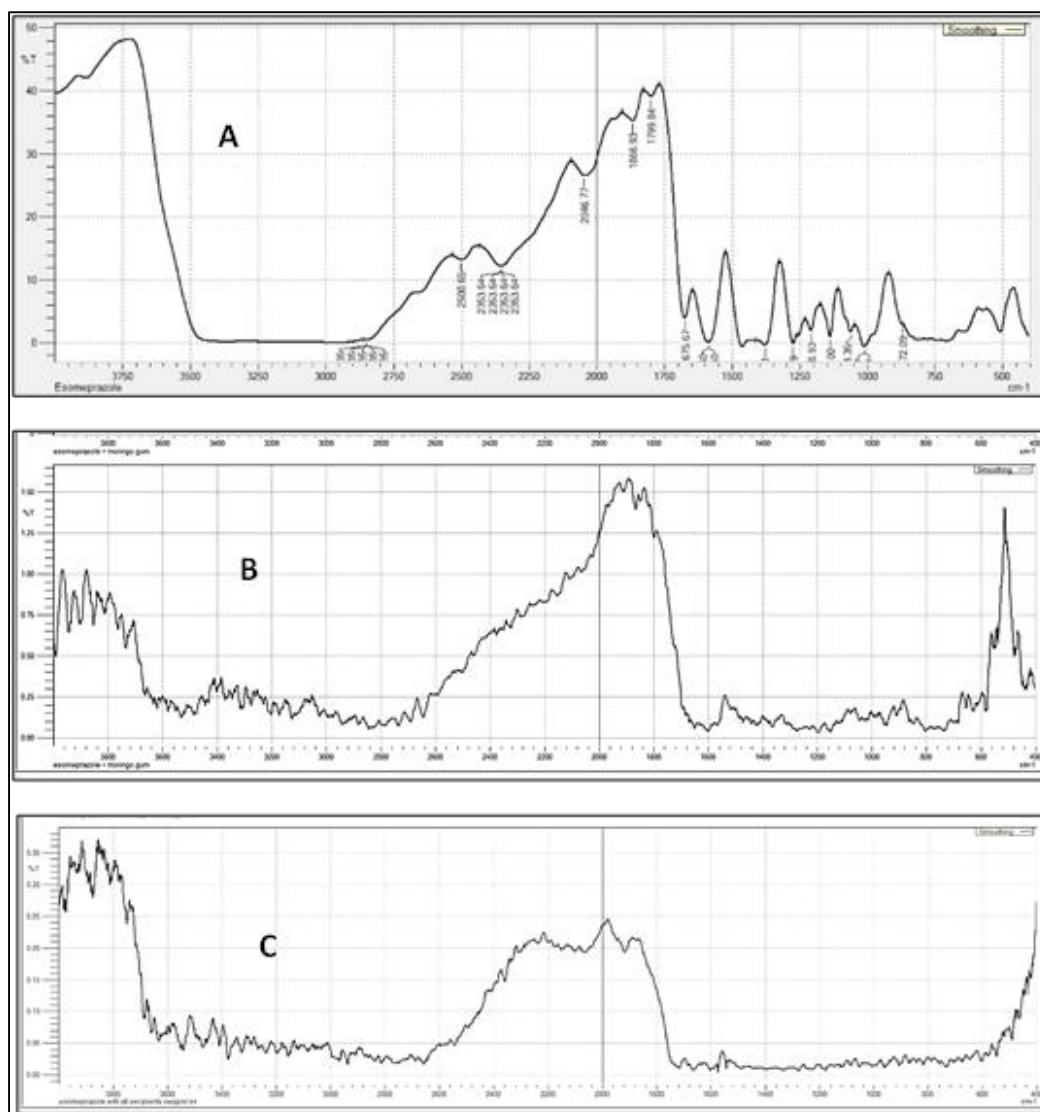


Figure 5 IR Spectra- (A)Esomeprazole magnesuium trihydrate, (B) Esomeprazole+ Moringa Gum, (C) Esomeprazole + all excipients

Table 4 Precompression parameters of Esomeprazole floating tablet

Formulation	Angle of repose (°)	Bulk density (g/ml)	Tapped density (g/ml)	Carr's index	Hausner's ratio
F1	38.21	0.57	0.72	20.83	1.26
F2	33.15	0.62	0.73	15.06	1.17
F3	36.40	0.56	0.66	15.15	1.17
F4	32.12	0.61	0.71	14.08	1.16

According to the aforementioned statistics, the tapped density varied from 0.66 to 0.73 (g/ml), while the bulk density for all formulations ranged from 0.56 to 0.62 (g/ml). The powder blend's angle of repose was found to be within the satisfactory or acceptable range in all formulations, ranging from 32.12° to 38.21°. This suggests that the powder blend possesses the necessary flowability to allow for sufficient flow into the die cavity. For the best powder blend flow, the powder blend's Carr's index for all formulations ranged from 14.08 to 20.83%, suggesting good to acceptable

flowability. It was discovered that the Hausner ratio ranged from 1.16 to 1.26. The powder mixture had a satisfactory powder flow, according to all of these statistics.

3.3. Post-compression Evaluation

The final floating tablet formulation was evaluated for weight fluctuation, hardness, thickness, and % friability. The physical parameters were found to be within the pharmacopeial limitations, as indicated by the results. The generation and entrapment of carbon dioxide gas within the swelling gel was caused by the interaction of acidic fluid and sodium bicarbonate when the dissolving media was absorbed into the matrix. This phenomenon caused floating as the matrix volume grew and density dropped. Therefore, the floating system was selected to ensure the smallest feasible lag time and a floating lifetime of more than 12 hours, all while compromising matrix integrity. After being submerged in 500 cc of 0.1 N HCl at 37 ± 0.5 °C for 23 seconds, the tablets floated and continued to float throughout the dissolution process.

Table 5 Physical parameters of Esomeprazole tablet

Batches	Hardness(kg/cm ²)	Thickness (mm)	% Friability	Wt. variation	F _{lag} (sec)(FLT)	Floating time (h)
F1	5.5	4.41	0.437	95.15	10	12
F2	5	4.045	0.440	95.08	15	12
F3	5	4.416	0.432	95.75	12	12
F4	4.5	4.261	0.430	96.05	13	12

3.4. Swelling Study

The polymer's hydrophilicity allows it to absorb water, which causes the tablet to swell. As a result, swelling gets worse with time due to the polymer's hydrophilicity. The optimized batch's swelling index is provided below.

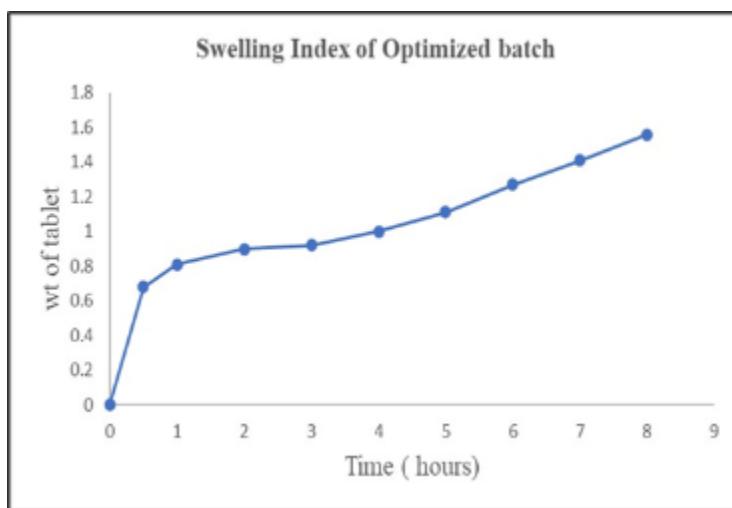


Figure 6 Swelling Study of optimized batch

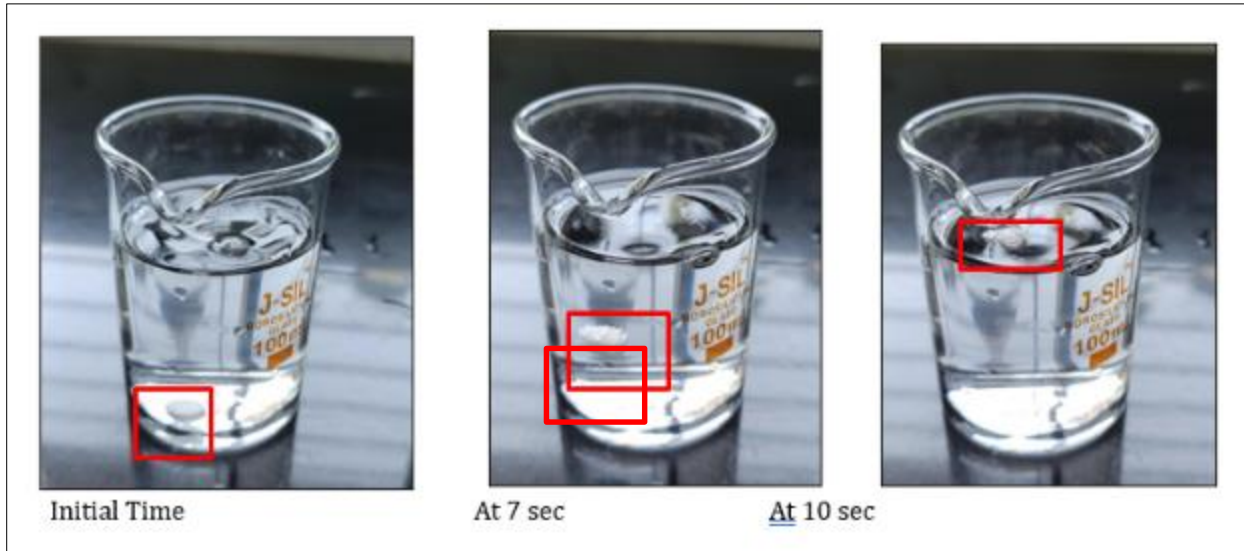


Figure 7 Visual depiction of a floating tablet's buoyancy

3.5. In-Vitro Dissolution

In an acidic environment (pH 1.2), the floating tablet demonstrated a sustained release of the medication, and it was discovered that this release was roughly linear. At first, 95–96% of the medication was released. Moreover, the polymer regulated the medication release from the floating tablet. The purpose of the dissolution study is to examine the drug release patterns of floating tablets that contain sodium alginate, xanthan gum, neem gum, and moringa gum. Comprehending these profiles is essential to guaranteeing uniform therapeutic results and refining the formulation. 96% of the medication was released over eight hours, according to the drug release profiles, demonstrating a more consistent and regulated release from Moringa gum tablets. Comparatively, the medication was released 89% by neem gum pills in 9 hours, and 93% by xanthan gum tablets in the same amount of time..

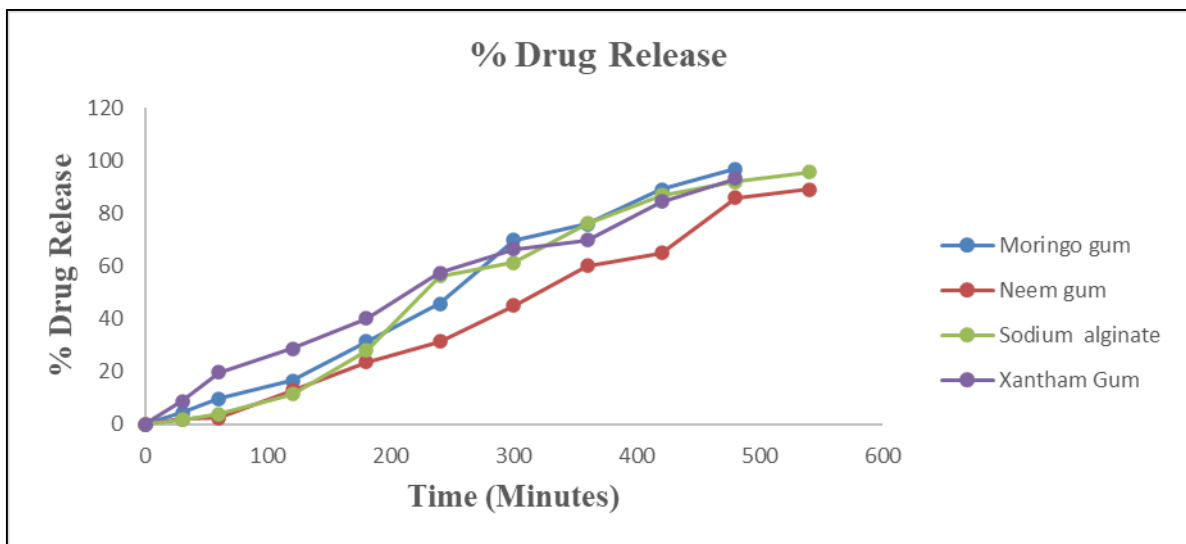


Figure 8 *In-vitro* dissolution study of all batches

4. Conclusion

In present work step by step studies were carried out to develop and optimize oral floating tablet for Esomeprazole using hydrophilic polymers. The floating tablets were prepared by direct compression technique it may be concluded from the present study that slow and sustained release of Esomeprazole over a period of 12 hr was obtained (F1 to F4) by the using Moringa gum, Azadirachta indica gum, Sodium alginate was successful in the formulation of floating tablet and at the same time it is effective in retarding the drug release. Moringa gum provides a superior dissolution profile for floating tablets, making it a promising excipient for achieving controlled and consistent drug release. This study suggests that Moringa gum could be effectively utilized in gastroretentive drug delivery systems. The drug release profiles showed that Moringa gum tablets had a more consistent and controlled release, with 96% of the drug released over 8 hours. In comparison, neem gum tablets released 89% of the drug within 9 hours, xanthan gum tablets released 93% over 8 hours, and sodium alginate tablets released 96% over 9 hours. Moringa gum's superior performance can be attributed to its balanced gel-forming ability, which maintains a stable matrix for controlled drug release. Neem gum, with its weaker gel matrix, resulted in faster erosion and less controlled release. Xanthan gum's strong gel excessively retarded drug release, while sodium alginate's dense gel also slowed the release rate too much.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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