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Formulation of Esomeprazole Sustained Release Tablets Using Natural Polymers

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ABSTRACT

The objective of present study is to prepare and evaluate sustained release tablets using natural polymers to modify and improve the drug performance and to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of single dose. Sustained release drug delivery system optimizes the pharmacodynamics and biopharmaceutical properties of a drug. Esomeprazole is a proton pump inhibitor and is the s-isomer of Omeprazole that inhibits gastric acid secretion and is used in the treatment of GERD, and in the healing of erosive esophagitis, and H. pylori eradication to reduce the risk of duodenal ulcer recurrence. The tablets were prepared by direct compression method using PVP K30, microcrystalline cellulose, guar gum and pectin as polymers. The tablets were evaluated for their micromeritic properties, release kinetic pattern, stability studies and in-vitro release by Fourier transform infrared (FTIR). The data obtained by FTIR indicates that the sustainability of the drug with Guar gum as a sustaining polymer at a concentration of 60 mg was found to show good sustainability when compared to all other formulations, as it showed 99 % drug release for 24 hrs. The optimized formulation dissolution data was subjected to release kinetics. From the release kinetics data, it was evident that the formulation followed Higuchi mechanism of drug release. The success of the *in-vitro* drug release and polymer compatibility studies recommends the product for further *in-vivo* studies, it may improve patient compliance.

INTRODUCTION

The oral route remains the most considered route for the administration of various types of drugs and tablets.[1]The oral route of administration for sustained release systems has received greater attention because of more flexibility in dosage form design. The design of oral sustained release delivery systems is subjected to several interrelated variables of considerable importance such as the type of delivery system.[2] Sustained release dosage forms are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after the administration of single dose. The main aim of preparing sustained release formulations was intended to modify and improve the drug performance by increasing the duration of drug action, decreasing the frequency of dosing, decreasing the required dose employed and providing uniform drug delivery.[3]

Sustained release dosage forms are prepared by coating the tablets so that the rate of solubility is controlled or individually encapsulating micro-particles of varying sizes so that the rate of dissolution can be controlled. Sustained release drug delivery system reduces the toxicity by slowing drug absorption, improved palatability, and availability of formulation in liquid and solid dosage form. Sustained release drug delivery system increases stability by protecting the drug from hydrolysis or other degradation changes in the gastrointestinal tract.[4]

The preparation of sustained release matrix tablets involves the direct compression of blend powder mixture of drug, retardant material and other additives to formulate a tablet in which the drug is dispersed in a matrix of the tablet. These systems continuously releases the drug by dissolution-controlled and diffusion-controlled mechanisms.[5]

Esomeprazole is a compound that inhibits gastric acid secretion and is indicated in the treatment of gastroesophageal reflux disease (GERD), the healing of erosive esophagitis, and H. pylori eradication to reduce the risk of duodenal ulcer recurrence.[6]Esomeprazole exerts its stomach acid-suppressing effects by preventing the final step in gastric acid production by covalently binding to sulfhydryl groups of cysteines found on the (H^+, K^+)-ATPase enzyme at the secretory surface of gastric parietal cells. This effect leads to inhibition of both basal and stimulated gastric acid secretion, irrespective of the stimulus. As the binding of esomeprazole to the (H+-ATPase, K+-ATPase) enzyme is irreversible and new enzyme needs to be expressed to resume acid secretion, esomeprazole's duration of antisecretory effect that persists longer than 24 hours.[7]

MATERIALS AND METHODS

Materials

Esomeprazole and Guar gum were procured from Mylan Laboratories, Hyderabad. PVP K30, Microcrystalline cellulose, Pectin, Talc, Magnesium stearate – Lubricant were purchased from Standard Chemicals. Manila copal was provided by Serin Formulations Private Limited. All other chemicals used in our work were of analytical grade.

Polymer Profile

Guar Gum

It is a naturally occurring galactomannan polysaccharide, it consists of chiefly high molecular weight hydrocolloidal polysaccharides, that are composed of galactan and mannan units combined through glycoside linkages and shows degradation in the large intestine due to the presence of microbial enzymes. [8]

Pectin

Pectin is an essentially linear polysaccharide, it is both polydisperse and polymolecular. Its composition varies with the source and the conditions applied during isolation. It also has several unique properties that have enabled it to be used as a matrix for the entrapment and/or delivery of a variety of drugs, proteins and cells. [9]

Povidone

Povidone is a synthetic polymer consisting essentially of linear1-vinyl-2-pyrrolidinone groups, it is characterized by its viscosity in aqueous solution, relative to that of water, expressed as a *K*-value, in the range 10 - 20. [10]

Microcrystalline cellulose

Microcrystalline cellulose is purified, partially depolymerized cellulose that occurs as a white, odourless, tasteless, crystalline powder composed of porous particles.[11] It is widely used in cosmetics, foods, and pharmaceutical formulations.[12]

Purified Talc

Talc is used as a lubricant in tablet formulations and in a novel powder coating for extended-release pellets and as an adsorbent. It was once widely used in oral solid dosage formulations as a lubricant and diluent.[13]

Magnesium stearate

Magnesium stearate is a very fine, light white, precipitated or milled, impalpable powder of low bulk density, having a faint odour of stearic acid and a characteristic taste. It is greasy to touch and readily adheres to the skin.[14] It is primarily used as a lubricant in capsule and tablet preperation at concentrations between 0.25 % and 5.0 % w/w.[15]

Equipments

Table 1: List of Instruments /Equipments

S. No.	Equipments	Modified/Manufacturer
1	Double rotary tablet compression Machine	Karunavati Pvt Ltd., Rajasthan (RIMEK Minipress)
2	Hardness tester, Pfizer	Mitutoyo South Asia Pvt Ltd., New Delhi
3	Friabilator	Roche Friabilator
4	pH meter	Shankar Scientific, Chennai
5	Dissolution Apparatus	Lab India Disso-2000
6	Double beam spectrophotometer	Shimadzu Scientific Instruments, Japan
7	FT-IR Spectrophotometer	Shimadzu Scientific Instruments, Japan

Methods

Formulation and preparation of tablets

Sustained release tablets were prepared by direct compression method, the drug and all other excipients except magnesium stearate and talc were weighed appropriately and were passed through sieve No.30. Magnesium stearate and talc were passed through mesh No.60. Esomeprazole was mixed with different ratios of PVP K30, guar gum, pectin,

microcrystalline cellulose for 10 min. The blend was mixed with magnesium stearate for 3-5 min and then it was compressed into tablets by utilizing direct compression method. The tablets were compressed using a double rotary tablet compression machine. The mass of the tablets were determined with the help of digital balance and thickness with the help of screw gauge. The composition of different formulas of esomeprazole sustained release tablets is shown in Table 2.

Table 2: Formulations for design of Sustained release tablets of Esomeprazole

Formulation code / compositions	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)	F10 (mg)	F11 (mg)	F12 (mg)
Esomeprazole	20	20	20	20	20	20	20	20	20	20	20	20
Manila Copal	10	20	40	60	-	-	-	-	-	-	-	-
Guar Gum	-	-	-	-	10	20	30	40	-	-	-	-
Pectin	-	-	-	-	-	-	-	-	10	20	30	40
Microcrystalline Cellulose	63.8	53.8	33.8	13.8	63.8	53.8	33.8	13.8	63.8	53.8	33.8	13.8
PVP K30	5	5	5	5	5	5	5	5	5	5	5	5
Talc	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Magnesium Stearate	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Total	100	100	100	100	100	100	100	100	100	100	100	100

Evaluation of Pre-Compression characteristics

Drug and excipients compatibility studies

FTIR spectroscopy was carried out for pure drug and polymers to know any chemical interactions between polymers and drug. The samples of pure drug, polymers and physical mixture of drug and polymers were dispersed in 200 mg of KBr powder and compressed into pellets at a pressure of 6000 kg/cm^2 and analyzed. Spectral measurements were obtained by powder diffuse reflectance on a FT-infrared spectrophotometer (Shimadzu, FT-IR, Japan) in the range 4000 – 400 cm^{-1}.[16]

Angle of Repose

The flow property was determined by measuring the Angle of Repose, It is the maximum angle that can be obtained between the free standing surface of a powder heap and the horizontal plane.

$$\theta = \tan^{-1}{}_{h/r}$$

Where,

h = height

r = radius

θ = angle of repose

Procedure

1. 20 gms of sample was taken.
2. The sample was passed through the funnel slowly to form a heap.
3. The height of the power heap formed was measured.
4. The circumference formed was drawn with a pencil on the graph paper.
5. The radius was measured and the angle of repose was determined. This was repeated three times for a sample.

Compressibility Index

The flow property was also determined by measuring the compressibility index (I) (flowability). A simple indication of the case with which a material can be induced to flow is given by the application of a compressibility index (I) given by equation.

$$I = [1 - (V/V_o)] \times 100$$

Where, V is the volume occupied by a sample of the powder after being subjected to a standardized tapping procedure (after 500 vibrations) and, V_o is the volume before tapping.

Procedure

1. 10 gm of the final blend was taken in a 50 ml measuring cylinder.

2. Measured the initial volume before tapping of the three measuring cylinders.

3. After 500 tapings, occupied volume was determined for each measuring cylinder.

4. The compressibility index (I) was determined by using the above equation.

Post compression characteristics of esomeprazole tablets

Weight Variation

The USP weight variation test was run by weighing 20 tablets individually, calculating the average weight, and comparing the individual tablet weights to the average. The tablets met the USP test that was no more than 2 tablets were outside the percentage limit and no tablets differed by more than 2 times the percentage limit.[17]

Table 3: Weight Variation Tolerance for Uncoated Tablets

S. No.	Average weight of tablets (mg)	Maximum percentage difference allowed
1	130 or less	10
2	130 to 324	7.5
3	More than 324	5

Hardness

Hardness of the tablets were determined by breaking it between the second and third fingers and thumb being as a fulcrum. There was a sharp snap the tablet was deemed to have acceptable strength.

Hardness of the tablets are also determined by Stokes Monsanto Hardness Tester and the hardness found within the range of 3.5-5.5 kg/cm².

Friability

The friability of tablets was determined by Roche friabilator. 20 tablets were taken and weighed. After weighing, the tablets were placed in the Roche friabilator and subjected to the combined effects of abrasion and shock by utilizing a plastic chamber that revolves at 25rpm/100 revolutions. In Roche Friabilator the tablets were dropped from a height of six inches with each revolution and after operation the tablets were deducted and reweighed.[18]

Friability is determined by F= 100 (1-Wo/Wt)

Where,

Wo= weight of tablets before friability test.

Wt= weight of tablets after friability test.

Content Uniformity

Five tablets were weighed and powdered, then its 10 mg was taken, weighed and dissolved in suitable quantity of methanol, the solution was filtered suitably diluted and then the drug content was analyzed using UV spectrometer at 300 nm.

***In-Vitro* Dissolution Studies of Esomeprazole Sustained Released Tablets**

Apparatus II (Paddle Method)

The same equipment as in apparatus I was used, expected that a paddle replaced the basket, formed from a blade and a shaft as a stirring element. The dosage form was allowed to sink to the bottom of the flask before stirring. A constant temperature of 37±0.5 ºC was maintained. The motor was adjusted to turn at the specified speed of 50 rpm, and the samples of the fluid were withdrawn at intervals to determine the amount of drug in solution.

Dissolution study of Esomeprazole Sustained Release Tablets

The dissolution test was carried out using USP apparatus II (Lab India Disso 2000). The stirring speed was maintained at 50 rpm. pH 6.8 phosphate buffer was used as dissolution medium (900 ml) and was maintained at 37±0.5°C. Samples of specified volume were withdrawn at predetermined time intervals, filtered, diluted suitably and assayed spectrophotometrically. An equal volume of fresh medium was immediately replaced to maintain the dissolution volume. The sample was analyzed spectrophotometrically at 300 nm.[19]

Kinetic Models

Release Kinetics

To analyse the mechanism for the drug release and drug release rate kinetics of the dosage form, the data obtained was fitted in Zero order and First order model. In this by comparing the R-values obtained, the best-fit model was selected.[20]

Zero Order Kinetics

This model describes the system where the release rate is independent of the concentration of the dissolved species.

The following relation can simply express this model.

$$\log Q_t = \log Q_o + K_o t$$

Where,

Qt= Amount of drug dissolved in time t.

Qo = Initial amount of drug in the solution.

K_o = Zero order release constant.

First Order Kinetics

The first order equation describes the release from systems where the dissolution rate is dependent upon the concentration of the dissolving species.

To study the first order release rate kinetics, the release rate data were fitted to the following equation.

$$\log Qt = \log Qo + K_1 t / 2.303$$

Where,

Qt =Amount of drug released in time t.

Qo = Initial amount of drug in the solution.

K_1 = First order release constant.

Higuchi Model

A large number of modified release dosage forms contain some sort of matrix system. In such instances, the drug dissolves from the matrix. The dissolution pattern of the drug is dictated by water penetration rate (diffusion controlled) and thus the following relationship applies as formula:

$$Q = k2\ t^{1/2}$$

Where Q is the percent of drug release at time t, and k2 is the diffusion rate constant.

In the Higuchi model, a plot of % drug released versus square root of time is linear.

Stability Studies

Short term stability studies were carried out for the optimized (F8) formulation. An adequate number of tablets were filled in amber coloured rubber stopper bottles and reserved in stability compartment maintained at a temperature of 40 ± 2ºC / 75 ± 5% RH for three months were analyzed regularly, for their physical appearance, friability, drug content, and *in-vitro* drug release.[21]

RESULT AND DISCUSSION

Esomeprazole exerts its stomach acid-suppressing effects by preventing the final step in gastric acid production by covalently binding to sulfhydryl groups of cysteines found on the (H^+, K^+)-ATPase enzyme at the secretory surface of gastric parietal cells. This effect leads to inhibition of both basal and stimulated gastric acid secretion, irrespective of the stimulus. Therefore formulating sustained release esomeprazole tablets extends the release up to 6 to 12 hrs. Esomeprazole sustained release tablets were prepared using direct compression method using polymers like guar gum, pectin, PVP K30.

Influence of Excipients

Tablets containing 65% pellets and 35% excipients in the form of powder were prepared by direct compression. Microcrystalline cellulose is mostly used as an excipient for the direct compression method because microcrystalline cellulose has good compaction and is consolidated by plastic deformation, which protects the coated particles better than other diluents.[22]

Pre-formulation Studies

Pre-formulation studies are done to investigate the physicochemical properties of the drug and to establish its compatibility with other excipients present in the formulation. The description of the drug was observed visually. The solubility data reveals that the drug is freely soluble and is a member of class III drugs according to the BCS classification. The loss on drying data was observed indicating that the API is non-hygroscopic. The melting point of the Esomeprazole was determined using the melting point apparatus. The particle size analysis was performed by the microscopic method.

Table 4: Pre-formulation study results of Esomeprazole

Sr. No.	Test	Specification	Results
1.	**Organoleptic properties**		
	Colour	White to off-white	White to off-white
	Odour	Odourless	Odourless
	Nature	Amorphous	Amorphous
2.	Solubility	slightly soluble in water	Slightly soluble in water
3.	LOD	NMT 0.5% of its Weight	0.25%
4.	Melting Point	155ºC	155ºC
5.	Assay	NLT 98.0% and NMT 102.0%	99.86%
6.	Particle size analysis	3-5 mm	4 mm

FT-IR Compatibility Studies

In FTIR spectra of pure drug with other ingredients, it is observed that the peaks of major functional groups of Esomeprazole, which are present in spectrum of pure drug are observed. It means that there are no interactions between drug and other ingredients and the drug is compatible with other ingredients.

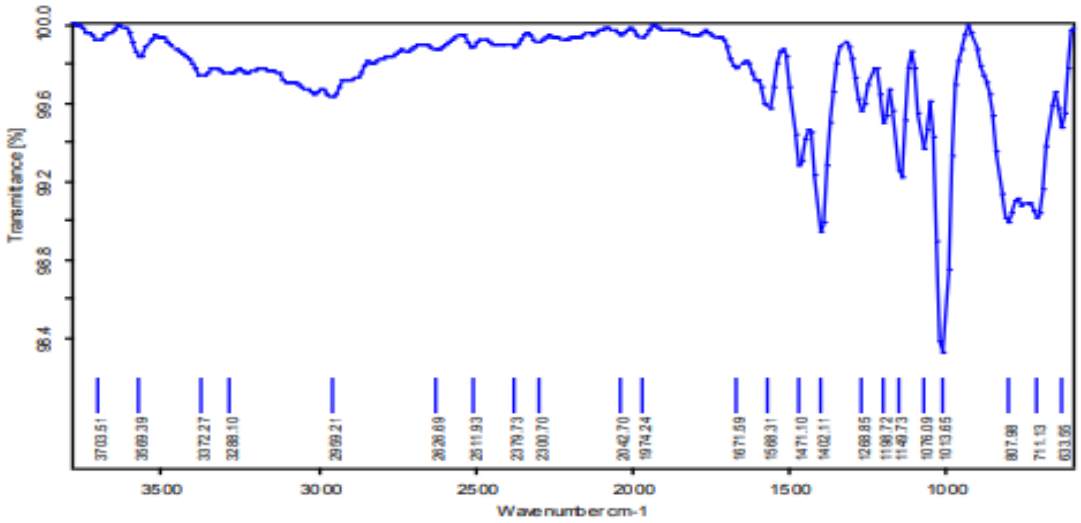

Figure 1: FT-IR spectra of pure Esomeprazole.

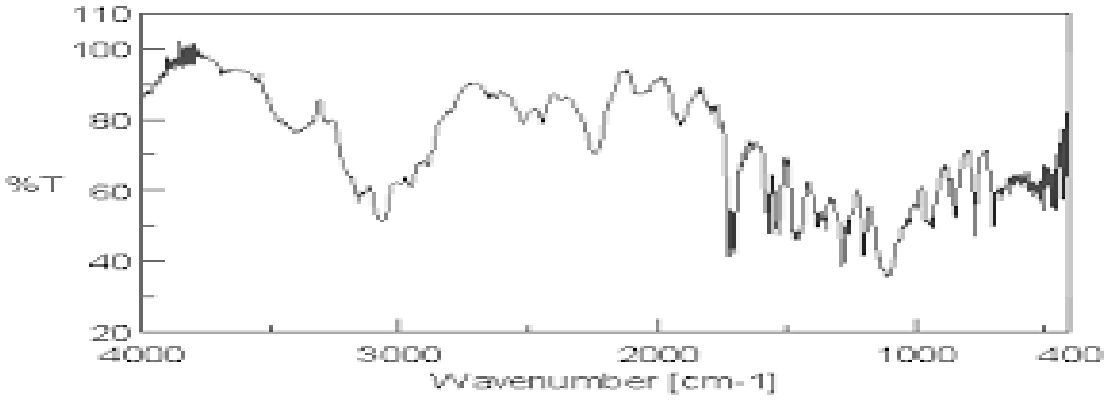

Figure 2: FT-IR spectra of physical mixture of Esomeprazole and polymers.

FT-IR spectra of pure drug is shown in Figure 2. The broad peak at 3897.44 cm^{-1} in the spectra of the pure drug corresponds to N-H (stretching). The peak at 1002.05cm^{-1} corresponds to S=0 (stretching), the peak at 1155.47cm^{-1} for C-O-C (stretching). The drug and polymers employed were found to be compatible as similar peaks were observed with minor differences shown in Figure 2.

Preparation of calibration curve for Esomeprazole

1 gm of Esomeprazole was dissolved in 100 ml of pH 6.8 buffer by slight shaking (1000 mg/ml). From the stock solution, suitable serial dilutions were made to get the concentrations of 1, 3, 5, 7 and 9 µg/ml in pH 6.8 phosphate buffer solutions.

Table 5: Calibration curve of Esomeprazole

S. No	Concentration (µg/ml)	Absorbance (λmax = 300 nm)
1	1	0.035
2	3	0.110
3	5	0.191
4	7	0.280
5	9	0.367

Determination of flow properties of Esomeprazole

The Flow indices Hausner's ratio and Compressibility index showed that API has a good flow. Consequently, direct compression was followed for the manufacture of sustained release tablets.

Table 6: Flow properties of Esomeprazole

S. No.	Parameter	Results
1	Bulk density (gm/cc)	0.55 gm/cc
2	Tapped Density (gm/cc)	0.64 gm/cc
3	Compressibility Index (%)	16.36%
4	Hausner's Ratio	1.16

Evaluation of Pre-formulation parameters

The λmax of Esomeprazole in pH 6.8 phosphate buffer was scanned and found to have the maximum absorbance at 300 nm. Standard graph of Esomeprazole in pH 6.8 phosphate buffer was plotted and regression was 0.997. The formulations were prepared with natural polymers like manila copal, guar gum and pectin and then evaluated. The angle of repose values obtained for the formulations ranged from 20.48 to 27.40, this indicates good flow property of the powder blends. The compressibility index values for the formulations ranged from 11.36 to 21.8. This also indicates the powder blend has good flow property.

Table 7: Results of Pre-formulation evaluation

Formulation code/Parameter	Bulk density	Tapped density	Angle of repose	Compressibility Index	Hausner's Ratio
F1	0.462 ±0.01	0.591±0.06	26.06±0.12	21.8	1.25
F2	0.469±0.01	0.561±0.02	25.42±0.98	21.39	1.19
F3	0.46±0.02	0.55±0.01	22.62±0.28	16.36	1.19
F4	0.59±0.05	0.68±0.04	29.19±1.20	13.04	1.15
F5	0.49±0.06	0.57±0.07	27.40±1.21	14.04	1.16
F6	0.48±0.02	0.55±0.06	26.06±0.90	12.72	1.14
F7	0.46±0.02	0.53±0.06	24.38±1.21	13.20	1.15
F8	0.43±0.04	0.49±0.04	23.72±1.23	12.24	1.14
F9	0.41±0.03	0.47±0.01	21.94±2.12	12.76	1.14
F10	0.39±0.02	0.44±0.02	20.48±1.33	11.36	1.12
F11	0.55±0.21	0.64±0,02	26.21±1.78	14.06	1.16
F12	0.53±0.02	0.61±0.02	25.74±1.23	13.11	1.15

Evaluation of post compression parameters

The total weight of each formulation was not maintained uniformly however the weight variation of the tablets was within the limits of 5%. The measured hardness of tablets in all batches was ranged from 3.0 – 3.2 kg/cm^2. Friability values were found to be less than 1% in all prepared formulations and considered to be satisfactory.

Table 8: Result of post compression parameters

Formulation code/Parameter	Hardness (N/mm^2)	Weight variation	Friability (%)	Content Uniformity
F1	3.0±0.02	PASS	0.18±0.02	99.17±1.5
F2	3.1±0.03	PASS	0.22±0.02	99.44±1.2
F3	3.0±0.71	PASS	0.43±0.04	98.64±2.8
F4	3.2±0.03	PASS	0.20±0.02	99.42±3.1
F5	3.0±0.06	PASS	0.19±0.08	99.17±2.8
F6	3.0±0.04	PASS	0.22±0.06	99.44±2.0
F7	3.0±0.03	PASS	0.45±0.04	99.64±2.6
F8	3.1±0.02	PASS	0.24±0.02	100.2±3.2
F9	3.2±0.01	PASS	0.38±0.04	99.89±4.2
F10	3.2±0.03	PASS	0.12±0.04	99.97±3.2
F11	3.1±0.04	PASS	0.24±0.02	99.24±2.1
F12	3.0±0.04	PASS	0.16±0.03	99.62±1.2

Table 9: *In-vitro* evaluation percentage of drug results

Time (hr)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	F7 (%)	F8 (%)	F9 (%)	F10 (%)	F11 (%)	F12 (%)
1	42±1.2	43±2.2	31±1.1	32±1.8	42±2.4	33±2.1	26±1.5	22±1.8	46±1.9	44±1.0	36±2.4	32±2.6
2	54±1.0	54±2.8	43±1.2	38±1.4	56±3.3	43±2.0	38±1.7	32±4.3	57±2.2	58±1.1	43±1.7	41±2.2
4	65±3.1	61±2.2	52±1.4	46±1.7	61±3.4	57±4.8	46±1.1	41±2.2	67±3.3	66±1.3	55±1.3	51±2.0
6	72±2.9	69±2.6	64±1.0	58±2.1	68±3.3	65±3.2	52±1.2	48±1.2	76±2.1	72±2.2	67±2.4	63±2.8
8	86±2.2	76±2.4	67±1.9	66±2.2	75±3.9	72±2.1	64±2.1	56±3.1	93±1.8	86±2.8	74±3.2	69±1.8
10	92±1.1	84±2.9	82±1.1	72±2.8	86±3.5	83±2.2	76±2.9	62±3.4	98±1.2	95±3.1	85±3.8	82±1.4
12	97±3.2	93±3.0	89±1.3	85±2.2	93±2.2	89±3.5	83±2.7	69±2.8		98±2.1	94±0.8	89±3.1
14		98±3.8	93±1.8	92±2.3	98±0.1	94±3.3	88±2.2	74±1.2			98±1.8	93±3.3
16			98±1.8	94±2.9		98±3.2	92±2.1	82±1.1				95±2.3
18				97±1.1			95±0.2	90±0.4				97±2.1
20							98±1.1	93±1.9				
22								97±0.9				
24								99±1.0				

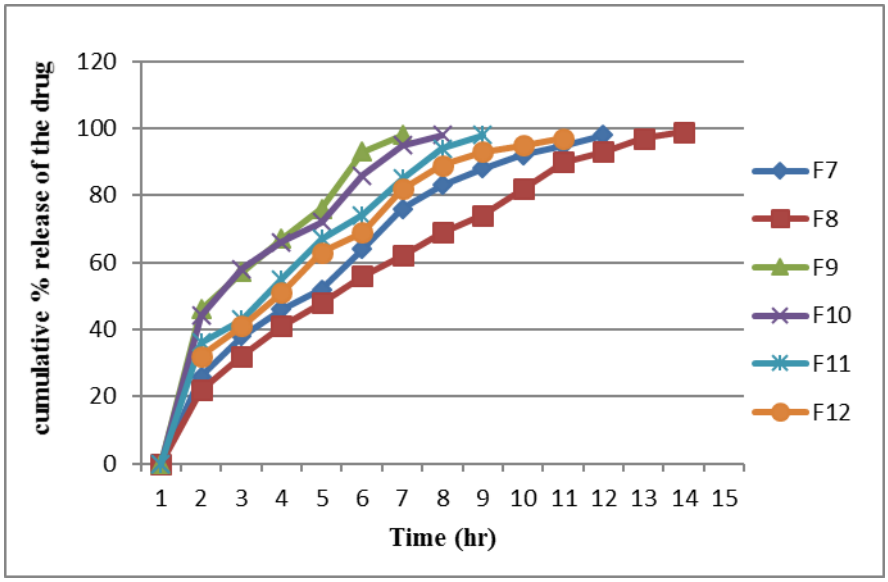

Figure 3: Cumulative percentage of *in-vitro* drug release (F1-F6)

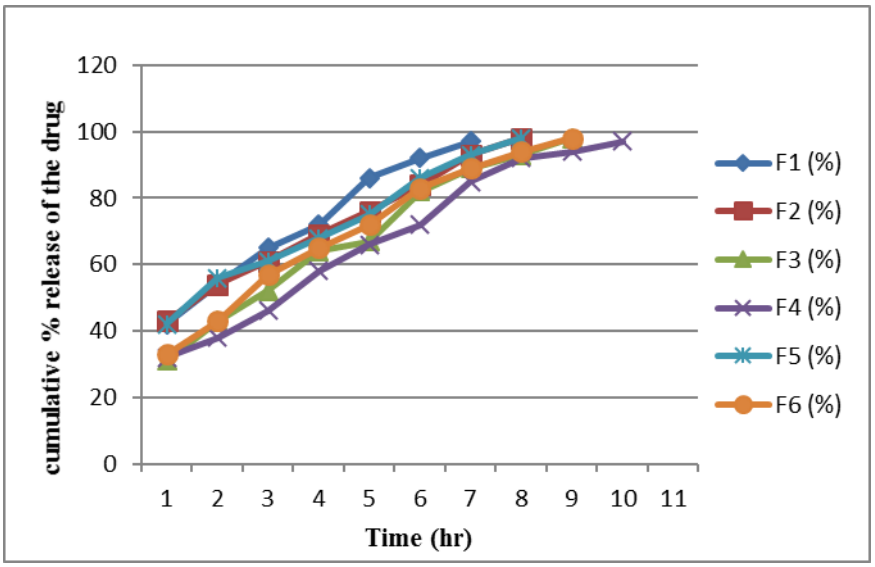

Figure 4: Cumulative percentage of *in-vitro* drug release (F6-F12)

Determination of *in-vitro* drug release pattern

In-vitro drug release profiles for all formulations were carried out by using 6.8 pH phosphate buffer as a dissolution medium for about 24 hrs. From the above results, it was found that the release of drug from formulation F8 which was composed of Guar gum at 60 mg gave the better release, drug content, friability, hardness than other formulations. The drug release from all the formulations followed the Higuchi model. The Correlation Coefficients (R^2) for the Higuchi model of drug release for the formulations are in the range of 0.921 to 0.995. The Higuchi plot between amounts of drug released as a function of the square root of time. The

amount of drug released from the formulation F6, F7, and F8 increased linearly with the square root of time indicating that the diffusion of the drug from the tablets, which is affected by the porosity and tortuosity of the matrix may be the rate-limiting step in the release of Esomeprazole from SR tablets.

Table 10: Release kinetic pattern of formulations

Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Zero-order (R2)	0.496	0.417	0.667	0.698	0.417	0.609	0.705	0.775	0.529	0.449	0.589	0.612
First order (R2)	0.959	0.9	0.966	0.939	0.905	0.973	0.975	0.981	0.925	0.94	0.977	0.983
Higuchi order (R2)	0.949	0.924	0.984	0.983	0.921	0.982	0.989	0.995	0.948	0.931	0.979	0.988

Stability studies of optimized formulation

The stability study results of optimized formulation F8 reflect that there is no significant change in physical appearance, friability, drug content and dissolution profile of the formulation. Hence, it concludes that the tablets from this formulation are stable for 3 months at 40 ±2°C.

Table 11: Stability studies of optimized formulation (F8)

Parameters	After 30 Days	After 60 Days	After 90 Days
Physical appearance	No Change	No Change	No Change
Friability	0.25±0.04	0.33±0.09	0.34±0.07
Drug content	101.70±0.47	99.63±0.116	99.13±0.101
In-vitro drug release	99.57±0.53	100.49±0.55	99.43±0.79

SUMMARY AND CONCLUSION

Esomeprazole is a proton pump inhibitor used in dyspepsia. The approach of the present study was to make a comparative evaluation among a concentration of Natural polymers like

guar gum and pectin and to assess the effect of physicochemical nature of the active ingredients on the drug release profile. The angle of repose, compressibility index results shown that the formulation is suitable for direct compression. This study showed that esomeprazole could be used in sustained release drug delivery system by formulating it as it has sustained drug delivery system which provides the extended duration of action in therapeutic range without reaching toxic levels as in the case of conventional dosage forms. These dosage forms have the ability to reduce the dosing frequency. The technique employed in the preparation of matrix system i.e. direct compression method is highly practical and economical from the industry point of view. The sustainability of the drug with Guar gum as a sustaining polymer at a concentration of 60 mg was found to show good sustainability when compared to all other formulation, as it showed 99% drug release for 24 hrs. The optimized formulation dissolution data was subjected to release kinetics. From the release kinetics data, it was evident that the formulation followed Higuchi mechanism of drug release. The success of the *in-vitro* drug release studies recommends the product for further *in vivo* studies, which may improve patient compliance.

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Conflict of Interest

The authors declare that they have no conflicts of interest to disclose.

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