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Formulation and evaluation of gastro retentive floating tablets of Perindopril Erbumine by using natural polymers

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ABSTRACT

The present study was carried out with an objective of preparation and *in vitro* evaluation of floating tablets of Perindopril Erbumine by using Tragacanth, Acacia Gum and Karayagum. The floating tablets were based on effervescent approach using sodium bicarbonate a gas generating agent. The formulated tablets were investigated for the quality control tests such as weight variation, hardness, friability, floating lag time and total floating time. The *in vitro* release study of the tablets was performed in 0.1 N HCl as a dissolution media. The results of the present study clearly indicates the promising potential of Perindopril Erbumine floating system as an alternative to the conventional dosage and other sustained release formulations. The drug release of optimized formulation was found to follow zero order kinetic models and r^2 value nearer to one and n value was found to be 0.985. Formulation PE4 exhibited better Gastroretentive controlled drug release in comparison to other prepared formulation.

Keywords: Febuxostat, Gum Copal, Isapgol husk, Fenugreek extract and Floating tablets.

1. INTRODUCTION

Oral delivery of drugs is the most preferable route of drug delivery. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient compliance and flexibility in formulation and cost effective manufacturing process [1]. Many of the drug delivery systems, available in the market are oral drug delivery type systems Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as:

a. Drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance.

b. A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.

c. The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the Css values fall or rise beyond the therapeutic range.

d. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overmedication occurs.[2]

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system that could revolutionize method of medication and provide a number of therapeutic benefits.[3]

The oral route is increasingly being used for the d elivery of therapeutic agents becausethe low cost of the

therapy and ease of administration lead to high le vels of patient compliance. More than 50% of the drugdelivery systems available in the market are o ral drugdelivery systems[4,5,6]. The successful develo pment of oral controlled drug delivery systems re quires an understanding of the

three aspects of the system, namely.

- The physiochemical characteristics of the dru g
- 2.Anatomy and physiology of GIT and Charac teristics of Dosage forms.

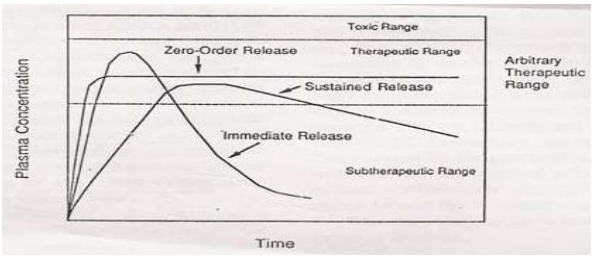


Figure – 1: Drug level verses time profile showing differences between zero order, controlled releases, slow first order sustained release and release from conventional tablet

Oral drug delivery systems have progressed from immediate release to site-specific delivery over a period of time. Every patient would always like to have a ideal drug delivery system possessing the two main properties that are single dose or less frequent dosing for the whole duration of treatment and the dosage form must release active drug directly at the site of action.[7]

1.1. Gastrointestinal retention

Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prol onged gastric retention improves bioavailability, r educes drug waste, and improves solubility for dr ugs that are less soluble in a high pH environment. Gastro retention helps to provide better availa bility of new products with new therapeutic pos sibilities and substantial benefits for patients5. To successfully modulate the gastrointestinal transi t time of a drug delivery systemthrough floating drug delivery system (FDDS) For maximal gast rointestinal absorption of drugs andsitespecific delivery, on needs to have a good fundamental understanding ofthe anatomic and physiological characteristics of the human GIT. **[8,9,10]**

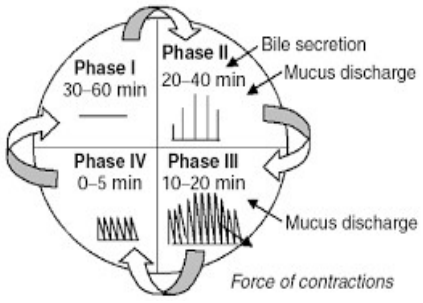


Figure – 2: Motility pattern in GIT

1.2. Gastroretentive Drug Delivery Systems

Gastroretentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients.[11]

1.3. Need For Gastroretentive Drug Delivery System

Various drugs have their greatest therapeutic effect when released in the stomach, particularly when the release is prolonged in a continuous, controlled manner. Drugs delivered in this manner have a lower level of side effects and provide their therapeutic effects without the need for repeated dosages or with a low dosage frequency. Sustained release in the stomach is also useful for therapeutic agents that the stomach does not readily absorb, since sustained release prolongs the contact time of the agent in the stomach or in the upper part of the small intestine, which is where absorption occurs and contact time is limited. Under normal or average conditions, for example, material passes through the small intestine in as little as 1-3 hours. Gastroretentive systems useful for drugs acting locally in the stomach (Antacids and drugs for H. Pylori viz., Misoprostol), Drugs that are primarily absorbed in the stomach (Amoxicillin), Drugs that is poorly soluble at alkaline pH (Furosemide, Diazepam, Verapamil), Drugs having narrow absorption window (Cyclosporine, Methotrexate, Levodopa), Drugs which are absorbed rapidly from the GI tract (Metonidazole, tetracycline), Drugs that degrade in the colon (Ranitidine, Metformin HCl), Drugs that disturb normal colonic microbes (antibiotics against Helicobacter pylori).[12,13]

1.4. Factors Controlling Gastroretention of Dosage Forms

The stomach anatomy and physiology contain parameters to be considered in the development of gastroretentive dosage forms. To pass through the pyloric valve in to the small intestine, the particle size should be in the range of 1 to 2 mm.[14] The most important parameters controlling the gastric retention time (GRT) of oral dosage forms include : density, size and shape of the dosage form, food intake and its nature, caloric content and frequency of intake, posture, gender, age, sex, sleep, body mass index, physical activity and diseased states of the individual (e.g. chronic

disease, diabetes etc.) and administration of drugs with impact on gastrointestinal transit time for example drugs acting as anticholinergic agents (e.g. atropine, propantheline), Opiates (e.g. codeine) and prokinetic agents (e.g. metclopramide, cisapride). The molecular weight and lipophilicity of the drug depending on its ionization state are also important parameters.[15]

1.5. Types of gastroretentive system

a. High Density System: Sedimentation has been employed as a retention mechanism for pellets that are small enough to be retained in the folds of the stomach body near the pyloric region, which is the part of the organ with the lowest position in an upright posture.[16]

b. Modified Shape Systems/ Unfolding Systems: These are the dosage forms, which after swallowing, swell to an extent that prevent their exit from the pylorus. As a result, the dosage form is retained for a longer period of time.[17]

c. Mucoadhesive Systems : Bioadhesive drug delivery systems are used as a delivery device within the human to enhance drug absorption in a site-specific manner. In this approach, bio adhesive polymers are used and they can adhere to the epithelial surface in the stomach. Thus, they improve the prolongation of gastricretention.[18] Materials commonly used for bioadhesion are poly acrylic acid, chitosan, cholestyramine, sodium alginate, hydroxypropyl methylcellulose (HPMC), sucralfate, tragacanth, dextrin, polyethylene glycol (PEG) and polylactic acids etc. Even though some of these polymers are effective at producing bioadhesive, it is very difficult to maintain it effectively because of the rapid turnover of mucus in the gastrointestinal tract (GIT).

d. Floating Drug Delivery System: Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time.

The drug usually keeps floating in th gastric fluid and slowly dissolves at a predetermined rate to release the drug from the dosage form and maintain constant drug levels in the blood [20]. Different approaches are currently used to prolong the gastric retention time, like hydro dynamically balanced systems, swelling and expanding systems, polymeric bio-adhesive systems, modified shape systems, high density systems and other delayed gastric emptying devices. The principle of buoyant preparation offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release [21].

1.6. Based on the mechanism of buoyancy two distinctly different technologies

- Non-effervescent system
- Effervescent system

Non-effervescent system

In this system commonly used excipients are gel-forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming polymers such as polycarbonate, polyacrylate, polymethacrylate and polystyrene. One of the approaches to the formulation of such floating dosage forms involves intimate mixing of drug with a gel forming hydrocolloid which swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and a bulk density of less than unity within the outer gelatinous barrier. The air entrapped by the swollen polymer confers buoyancy to these dosage forms. The gel structure acts as a reservoir for sustained drug release since the drug is slowly released for sustained drug release since the drug is slowly released by a controlled diffusion through the gelatinous barrier [22].

Effervescent system

These floating systems are prepared with swellable polymers such as methocel or polysaccharides like chitiosan and effervescent component containin sodium bicarbonate, citric and/or tartaric acid or matrices containing chambers of liquid that gasify at body temperature. The matrices are fabricated so that upon contact with gastric fluid, carbon dioxide is liberated by the acidity of gastric contents and is entrapped in the gelyfied hydrocolloid. This produces an upward motion of the dosage form and maintains its buoyancy. The carbon dioxide generating components may be intimately mixed within the tablet matrix to produce a single-layered tablet or a bi-layered tablet may be compressed which contains the gas generating mechanism in one hydrocolloid containing layer and the drug in the other layer formulated for the prolonged release effect [23].

Mechanism of floating systems

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. FDDS have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an

increased GRT and a better control of the fluctuations in plasma drug concentration [24].

However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature6. The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to maintain the submerged object. The object floats better if F is on the higher positive side [25]

F = F buoyancy - F gravity = (Df - Ds) gv

Where,

F= total vertical force;

Df = fluid density;

Ds = object density;

v = volume and g = acceleration due to gravity

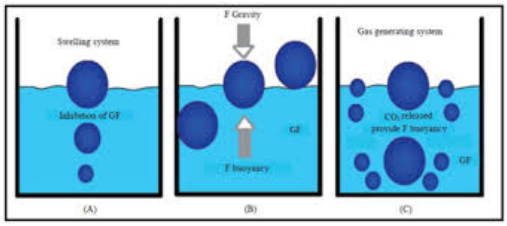


Figure – 3: Mechanism of floating systems

Suitable drug candidates for FDDS

Various drugs have their greatest therapeutic effect when released in the stomach, particularly when the release is prolonged in a continuous, controlled manner. In general, appropriate candidates for FDDS are molecules that have poor colonic absorption but are characterized by better absorption properties at the upper parts of the GIT [28]

- Drugs with narrow absorption window in GIT, e.g., Riboflavin and Levodopa
- Drugs that primarily absorbed from stomach and upper part of GIT, e.g., Calcium supplements, chlordiazepoxide and cinnarazine.
- Drugs that act locally in the stomach, e.g., Antacids and Misoprostol.
- Drugs that degrade in the colon, e.g., Ranitidine HCl and Metronidazole.
- Drugs that disturb normal colonic bacteria, e.g., Amoxicillin Trihydrate

Limitations of FDDS

1) Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted.

2) Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.

3) High variability in gastric emptying time due to its all or non-emptying process.

4) Gastric emptying of floating forms in supine subjects may occur at random and becomes highly dependent on the diameter and size. Therefore patients should not be dosed with floating forms just before going to bed.[29]

Polymers used in floating drug delivery [31,32]

Sustained Release Polymers are HPMC K100M, HPMC K15M, HPMC ELV, Polycarbonate, Polyethylene glycol, Sodium alginate, Carbopol, Eudragit.

Effervescent Generating System: Citric and Tartaric Acid, Sodium Bicarbonate,Citroglycine.

Polymers which increase buoyancy: Ethyl cellulose

Polymers which decrease release: Talc, Magnesium Stearate, Dicalcium Phosphate.

Polymers which increase release: Mannitol, Lactose.

Inert Polymers: Long Chain Fatty Alcohol, Fatty Acid, Beeswax.

Polymers with low density: Foam powder of polypropylene

2. MATERIALS AND METHODS

2.1. Analytical method development:

a) Determination of absorption maxima:

A solution containing theconcentration 10 µg/ mL drug was prepared in 0.1N HCL UV spectrum was taken using Double beam UV/VISspectrophotometer. The solution was scanned in the range of 200 – 400 nm.

b) Preparation calibration curve:

10mg Perindopril Erbumine pure drug was dissolved in 10ml of methanol (stock solution1) from stock solution 1ml of solution was taken and made up with10ml of 0.1N HCL (100µg/ml). From this 1ml was taken and made up with 10 ml of 0.1N HCL (10µg/ml). The above solution was subsequently diluted with 0.1N HCL to obtain series of dilutions Containing 2, 4, 6, 8, 10µg /ml of per ml of solution. The absorbance of the above dilutions was measured at 215 nm by using UV-Spectrophotometer taking 0.1N HCL as blank. Then a graph was plotted by taking Concentration

on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2)which determined by least-square linear regression analysis.

2.2. Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by thequality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Table - 1: Formulation composition for Floating tablets

Ingredients (MG)	Formulation Codes								
	PE1	PE2	PE3	PE4	PE5	PE6	PE7	PE8	PE9
Perindopril Erbumine	2	2	2	2	2	2	2	2	2
Tragacanth	10	20	30	-	-	-	-	-	-
Acacia Gum	-	-	-	10	20	30	-	-	-
Karayagum	-	-	-	-	-	-	10	20	30
Sodium bicarbonate	15	15	15	15	15	15	15	15	15
Citric acid	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Magnesium Stearate	4	4	4	4	4	4	4	4	4
Talc	5	5	5	5	5	5	5	5	5
Lactose	56.5	46.5	36.5	56.5	46.5	36.5	56.5	46.5	36.5
Total weight	100	100	100	100	100	100	100	100	100

All the quantities were in mg

2.2. Evaluation of post compression parameters for prepared Tablets

The designed compression tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation test:

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital variatweighing balance. The average weight of one tablet was determined from the collective weight. The weight ion test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined.The percent deviation was calculated using the following formula.

% Deviation = (Individual weight – Average weight / Average weight) × 100

Table -2: Pharmacopoeial specifications for tablet weight variation

Average weight of tablet (mg) (I.P)	Average weight of tablet (mg) (U.S.P)	Maximum percentage difference allowed
Less than 80	Less than 130	10
80-250	130-324	7.5
More than	More than 324	5

Hardness:

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation.

Thickness:

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

Friability:

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Pre weighed tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re-weighed, and loss in the weight of tablet is the measure of friability and is expressed in percentage as

% Friability = [(W1-W2) / W1] × 100

Where, W1 = Initial weight of tablets

W2 = Weight of the tablets after testing

Determination of drug content:

Both compression-coated tablets of were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to

one tablet weight of Perindopril Erbumine were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with water. The solution was suitably diluted and the absorption was determined by UV –Visible spectrophotometer. The drug concentration was calculated from the calibration curve.

***In vitro* Buoyancy studies:**

The in vitro buoyancy was determined by floating lag time, and total floating time. The tablets were placed in a 100ml beaker containing 0.1N HCL. The time required for the tablet to rise to the surface and float was determined as floating lag time (FLT) and duration of time the tablet constantly floats on the dissolution medium was noted as Total Floating Time respectively (TFT).

2.3. In vitro drug release studies

Dissolution parameters:

Apparatus -- USP-II, Paddle Method

Dissolution Medium -- 0.1 N HCL

RPM -- 50

Sampling intervals (hrs) -- 0.5,1,2,3,4,5,6,7,8,10,11,12

Temperature -- 37°c ± 0.5°c

As the preparation was for floating drug release given through oral route of administration, different receptors fluids are used for evaluation the dissolution profile.

Procedure:

900ml 0f 0.1 HCL was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°c ± 0.5°c. Tablet was placed in the vessel and the vessel was covered the apparatus was operated for 12 hours and then the medium 0.1 N HCL was taken and process was continued from 0 to 12 hrs at 50 rpm. At definite time intervals of 5 ml of the receptors fluid was withdrawn, filtered and again 5ml receptor fluid was replaced. Suitable dilutions were done with media and analyzed by spectrophotometrically at 215 nm using UV-spectrophotometer.

2.4. Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Zero order release rate kinetics:

To study the zero–order release kinetics the release rate data ar e fitted to the followingequation.

$F = K_o t$

Where, 'F' is the drug release at time't', and 'K_o' is the zero order release rateconstant. The plot of % drug release versus time is linear.

First order release rate kinetics:The release rate data are fitted to the following equation

Log (100-F) = kt

A plot of log cumulative percent of drug remaining to be released vs. time is plottedthen it gives first order release.

Higuchi release model: To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

F = k t1/2

Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

3. Results and Discussion

3.1. Analytical Method

a. Determination of absorption maxima

The standard curve is based on the spectrophotometer. The maximum absorption was observed at 215nm.

b. Calibration curve

Graphs of Perindopril Erbumine was taken in 0.1N HCL (pH 1.2)

Table - 3: Observations for graph of Perindopril Erbumine in 0.1N HCL

Concentration [µg/mL]	Abs
0	0
2	0.138
4	0.255
6	0.369
8	0.475
10	0.592

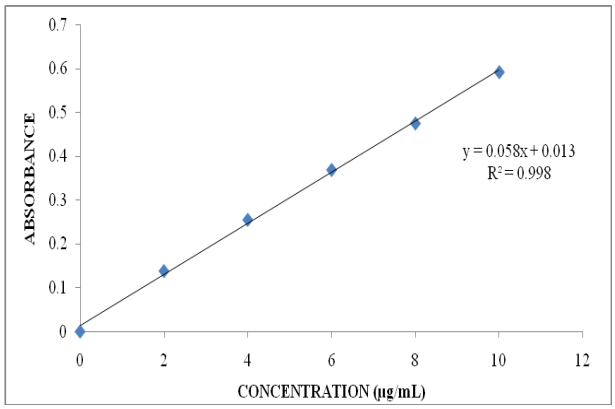


Figure - 4: Standard graph of Perindopril Erbumine in 0.1N HCL

Standard graph of Perindopril Erbumine was plotted as per the procedure in experimental method and its linearity is shown in Table 8.1 and Fig 8.1. The standard graph of Perindopril Erbumine showed good linearity with R^2 of 0.998, which indicates that it obeys "Beer- Lamberts" law.

Quality Control Parameters For tablets:

Tablet quality control tests such as weight variation, hardness, and friability, thickness, Drug content and drug release studies were performed for floating tablets. =

Preformulation parameters of powder blend:

Table 4: Pre-formulation parameters of blend

Formulation Code	Angle of Repose	Bulk density (gm/mL)	Tapped density (gm/mL)	Carr's index (%)	Hausner's Ratio
PE1	27°22±1.31	0.410±0.069	0.496±0.020	17.33±0.320	1.20±0.013
PE2	28°35±1.64	0.382±0.032	0.462±0.015	17.31±0.208	1.20±0.015
PE3	28°23±1.6	0.405±0.05	0.470±0.032	13.82±0.198	1.16±0.016
PE4	29°76±0.02	0.536±0.05	0.593±0.03	15.96±0.01	1.18±0.02
PE5	26°49±0.01	0.492±0.06	0.542±0.04	9.22±0.06	1.1±0.02
PE6	28°63±0.02	0.521±0.03	0.596±0.02	12.5±0.03	1.14±0.03
PE7	27°09±0.03	0.528±0.02	0.586±0.06	9.89±0.04	1.1±0.02
PE8	27°01±0.02	0.498±0.03	0.549±0.02	9.22±0.02	1.1±0.06
PE9	26°14±0.03	0.477±0.04	0.542±0.02	11.99±0.01	1.13±0.02

Table -5: *In vitro* quality control parameters

Formulation codes	Weight variation (mg)	Hardness (kg/cm²)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (sec)	Total Floating Time (Hrs)
PE1	95.24	5.2	0.35	3.69	98.76	43	10
PE2	99.38	5.8	0.28	3.81	97.53	51	12
PE3	98.41	5.2	0.35	3.79	95.28	42	12
PE4	96.75	6.0	0.68	3.15	99.18	20	12
PE5	99.12	5.4	0.59	3.86	96.30	42	11
PE6	98.67	5.9	0.42	3.79	98.43	38	12
PE7	97.25	5.4	0.78	3.95	97.35	24	11
PE8	99.82	5.2	0.60	3.46	99.12	52	12
PE9	98.71	5.5	0.52	3.57	98.76	30	12

All the parameters for SR layer such as weight variation, friability, hardness, thickness, drug content were found to be within limits.

***In vitro* drug release studies**

Table -6 : Dissolution data of Floating tablets

TIME (HR)	Cumulative Percentage of drug release								
	PE1	PE2	PE3	PE4	PE5	PE6	PE7	PE8	PE9
0	0	0	0	0	0	0	0	0	0
1	21.85	15.75	13.39	18.76	10.35	15.90	08.83	10.63	06.86
2	28.91	20.19	18.52	23.24	18.93	26.15	12.18	16.25	11.25
3	32.74	26.76	25.37	27.59	26.15	32.63	18.34	22.83	18.91
4	37.68	32.75	30.15	39.76	35.61	36.24	25.10	26.51	25.32
5	42.97	38.53	36.21	42.19	41.82	40.18	29.85	32.75	31.82
6	46.26	46.96	40.18	47.11	46.53	45.93	33.70	38.81	36.40
7	55.17	51.78	45.95	52.40	53.75	53.24	37.57	45.69	41.62

8	62.35	57.49	51.32	67.21	59.42	56.15	42.96	50.54	57.80
9	69.10	64.37	56.93	75.34	65.51	62.76	48.62	67.29	62.29
10	75.91	67.28	60.15	80.96	66.83	65.43	56.39	72.18	79.72
11	82.53	75.14	69.72	92.35	78.11	70.26	64.26	81.34	86.20
12	91.57	83.26	76.11	98.71	89.98	75.85	72.32	86.21	96.54

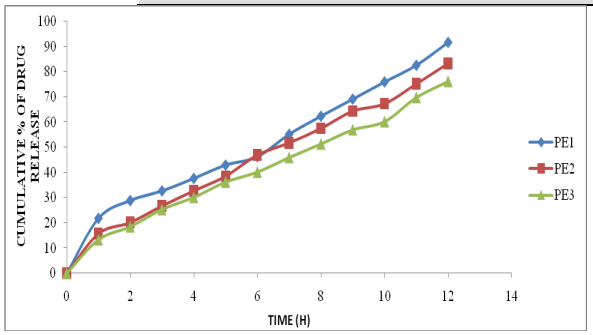


Figure - 5: Dissolution data of Perindopril Erbumine Floating tablets containing Tragacanth

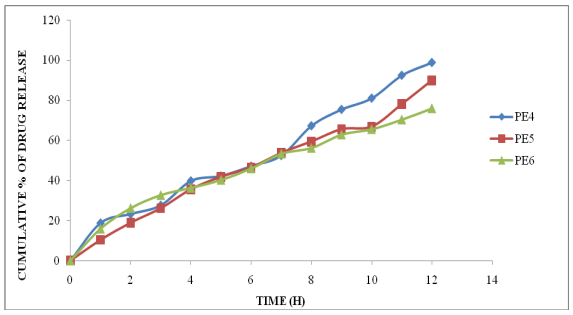


Figure - 6: Dissolution data of Perindopril Erbumine Floating tablets containing Acacia Gum

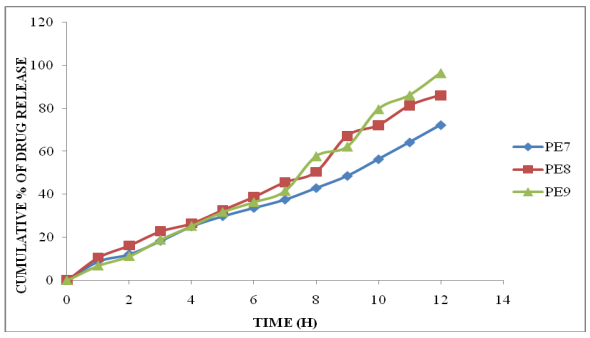


Figure - 7: Dissolution data of Perindopril Erbumine Floating tablets containing Karayagum

From the dissolution data it was evident that the formulations prepared with Tragacanth as polymer were retarded the drug release 12 hours.

Whereas the formulations prepared with low concentration of Acacia Gum retarded the drug release up to 12 hours in the concentration 10 mg. In higher concentrations the polymer was unable to retard the drug release.

Whereas the formulations prepared with Karayagum were retarded the drug release in the concentration of 30 mg (PE9 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 96.54 % in 12 hours with good retardation.

Hence from the above dissolution data it was concluded that PE4 formulation was considered as optimised formulation because good drug release (98.71%) in 12 hours.

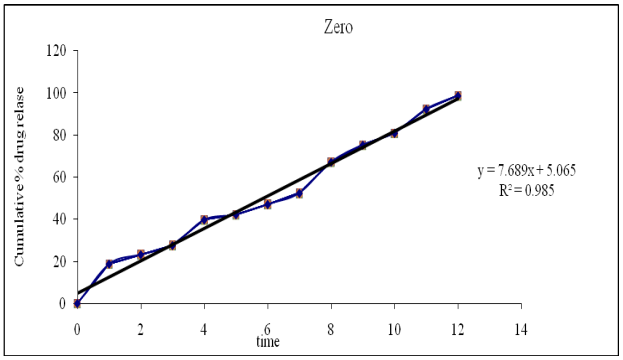


Figure -8 : Zero order release kinetics

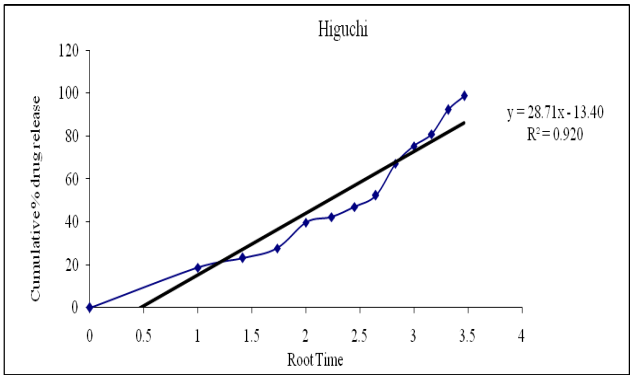


Figure - 9: Higuchi release kinetics

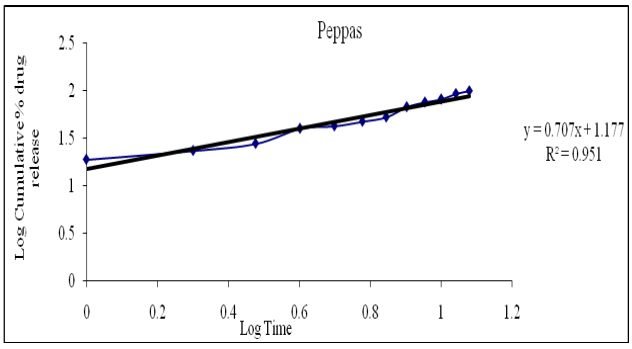


Figure - 9 : Kors mayer peppas release kinetics

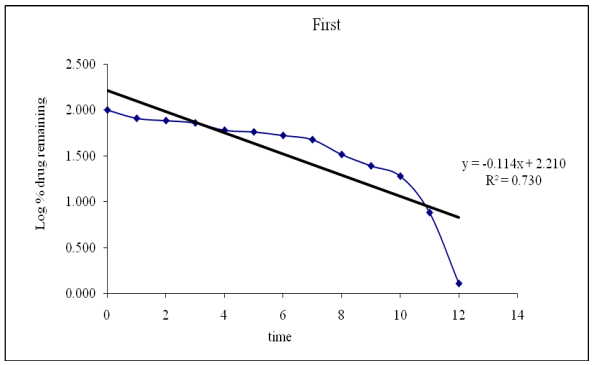


Figure - 10: First order release kinetics

Optimised formulation PE4 was kept for release kinetic studies. From the above graphs it was evident that the formulation PE4 was followed Zero order release kinetics mechanism.

Drug – Excipient compatability studies

Fourier Transform-Infrared Spectroscopy:

Figure8.11:FTIRSpectrum of pure drug

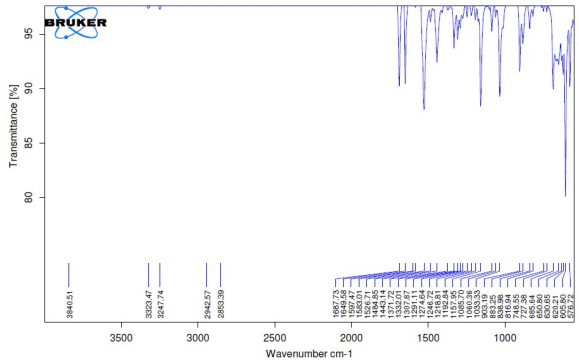
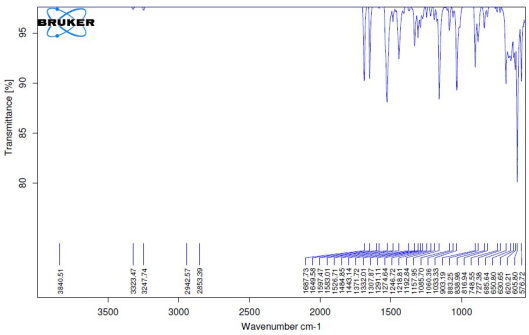


Fig 8.12 FTIR Spectrum of optimised formulation



There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.

Perindopril Erbumineare also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

The present study was carried out with an objective of preparation and *in vitro* evaluation of floating tablets of Perindopril Erbumine by using Tragacanth, Acacia Gum and Karayagum. The floating tablets were based on effervescent approach using sodium bicarbonate.

The formulated tablets were investigated for the quality control tests such as weight variation, hardness, friability, floating lag time and total floating time.

Table -7: The quality control parameters

Formulation codes	Weight variation (mg)	Hardness (kg/cm²)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (sec)	Total Floating Time (Hrs)
PE1	95.24	5.2	0.35	3.69	98.76	43	10
PE2	99.38	5.8	0.28	3.81	97.53	51	12
PE3	98.41	5.2	0.35	3.79	95.28	42	12
PE4	96.75	6.0	0.68	3.15	99.18	20	12
PE5	99.12	5.4	0.59	3.86	96.30	42	11
PE6	98.67	5.9	0.42	3.79	98.43	38	12
PE7	97.25	5.4	0.78	3.95	97.35	24	11
PE8	99.82	5.2	0.60	3.46	99.12	52	12
PE9	98.71	5.5	0.52	3.57	98.76	30	12

The *in vitro* release study of the tablets was performed in 0.1 N HCl as a dissolution media and the solution was scanned in the range of 200- 400 nm.

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.382±0.032 to 0.536±0.05 (gm/ml) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.462±0.015 to 0.596±0.02 showing the powder has good flow properties. The

compressibility index of all the formulations was found to be below 17.33 which shows that the powder has good flow properties.All the formulations has shown the Hausner's ratio ranging between 1.1 to 1.20 indicating the powder has good flow properties.

From the dissolution data the formulations prepared with Karayagum were retarded the drug release in the concentration of 30 mg (PE9 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 96.54 % in 12 hours with good retardation.

The drug release of optimized formulation was found to follow zero order kinetic models and r^2 value nearer to one and n value was found to be 0.985. Formulation PE4 exhibited better Gastroretentive controlled drug release in comparison to other prepared formulation.

5. CONCLUSION

The present study shows that Perindopril Erbumine can be made into floating tablet dosage form by direct compression technique. From the data obtained, it can be accomplished that, gastroretentive tablet of an Antihypertensive drug Perindopril Erbumine can be formulated as an advance to increase gastric residence time and thereby improve its bioavailability. Among the polymers used to improve the gastric residence, polymers (Tragacanth, Acacia Gum and Karayagum) showed better control over drug release. Formulated tablets gave satisfactory results for various physicochemical evaluations for tablets like hardness,Friability,ThicknessDrug content, weight variation, floating lag time, Total floating time, and *in vitro* drug release. Formulation PE4 exhibited better Gastroretentive controlled drug release in comparison to other prepared formulation. Formulated floating tablets best fitted to zero order kinetics.

The drug release of optimized formulation was found to follow zero order kinetic models and r^2 value nearer to one and n value was found to be 0.985. Formulation PE4 exhibited better Gastroretentive controlled drug release in comparison to other prepared formulation.

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