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FORMULATION DESIGN AND *IN VITRO* EVALUATION OF EPLERENONE GASTRORETENTIVE FLOATING MATRIX TABLETS FOR THE MANAGEMENT OF HYPERTENSION

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Abstract:
This study aimed to design and assess a hydrodynamically balanced floating matrix-controlled drug delivery system for Eplerenone. The elimination half-life of Eplerenone ranges from 3 to 6 hours. The gastric buoyancy of Eplerenone tablets is due to the effervescence generated by the reaction between sodium bicarbonate and hydrochloric acid in the stomach. Twelve distinct formulations of floating tablets were developed utilizing the direct compression method with hydrophilic polymers, including HPMC K4M, K15M, and K100M, alongside hydrophobic polymers such as Eudragit RSPO, in diverse ratios. The characterisation of the formulated preparation was conducted utilizing FTIR and DSC analyses. The evaluation results indicated that all formulations adhere to the specifications of official pharmacopoeias and/or standard references regarding general appearance, content consistency, hardness, friability, and buoyancy. Among all the formulations created, formulation EFT10, which comprises 25% HPMC K100M and 12.5% eudragit RSPO, demonstrated optimal in vitro drug release, achieving 99% at the conclusion of 12 hours. Formulations containing above 12.5% NaHCO3 exhibited a floating duration exceeding 12 hours. The kinetics of in vitro drug release for the improved formulation EFT10 exhibited zero-order kinetics, with a drug release mechanism characterized by anomalous diffusion combined with erosion. Accelerated stability experiments were conducted, revealing little alteration in physicochemical attributes and drug release profiles after 90 days, showing that all formulations remained stable.

Key words: *Gastroretensive drug delivery, floating drug delivery, Eplerenone, Eudragit RSPO, HPMC K4M, K15M, K100M*

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INTRODUCTION:

Gastroretentive drug delivery methods were developed to extend the residence duration of the medicine in the gastrointestinal tract. Gastric retention can be extended through the utilization of floating, mucoadhesive, swelling, and high-density systems. These devices provide the drug in gastric fluid over an extended duration before reaching its absorption site, thereby ensuring excellent bioavailability for medicines with stability and enhanced solubility in gastric fluids. Numerous strategies have been implemented over the past thirty years to enhance the retention of oral dose forms in the stomach. The predominant methods employed to enhance the gastric residence time of pharmaceutical dosage forms encompass a) co-administration of the drug delivery system with pharmacological agents that impede gastric motility, b) bioadhesive systems, c) size-increasing systems, achieved through expansion and shape modification, and d) density-controlled systems, which include either high-density or floating systems. Among the aforementioned approaches, floating devices for gastric retention are currently the most prevalent. Floating systems possess a lower density than gastric fluid, allowing them to remain buoyant in the stomach for an extended duration. As the system remains buoyant above the gastric contents, the medicine is gradually delivered at the specified rate. This leads to an extended gastric retention time and a reduction in plasma drug concentration variability[1]. Two unique technologies have been employed in the creation of FDDS based on the principle of buoyancy: A. Effervescent System, and B. Non-Effervescent System. Effervescent systems utilize gas-generating agents, such as carbonates (e.g., sodium bicarbonate) and various organic acids (e.g., citric acid and tartaric acid) in the formulation to generate carbon dioxide (CO2) gas, thereby decreasing the system's density and enabling it to float on gastric fluid. The non-effervescent FDDS operates on the principles of polymer swelling or bioadhesion to the mucosal layer within the gastrointestinal tract. The predominant excipients in non-effervescent FDDS include gel-forming or highly swellable cellulose-based hydrocolloids, polysaccharides, and matrix-forming substances such as polycarbonate, polyacrylate, polymethacrylate, polystyrene, along with bioadhesive polymers like chitosan and carbopol. Floating matrix tablets are a form of sustained-release drug delivery method that remain buoyant in stomach fluids for an extended duration by producing CO2 gas or by swelling to release the medicine over an extended timeframe. The extension of drug release can be accomplished through the utilization of diverse polymers, including various grades of HPMC, Eudragit, chitosan, Carbopol, guar gum, and xanthan gum[2].

Hypertension, or high blood pressure, is a chronic medical disorder characterized by consistently raised arterial blood pressure. Hypertension typically does not manifest symptoms on its own[3]. It is, nonetheless, a significant risk factor for stroke, coronary artery disease, heart failure, atrial fibrillation, peripheral arterial disease, visual impairment, chronic renal disease, and dementia. Hypertension is a significant contributor to early mortality globally[4]. Eplerenone is an antihypertensive medicine that is a member of the mineralocorticoid receptor antagonist pharmacological class. Eplerenone is well absorbed when taken orally, reaching its peak plasma concentration in about an hour. Eplerenone has an elimination half-life of roughly 4 to 6 hours[5]. Alpha l-acid glycoproteins make up the majority of plasma proteins, which bind about 50% of eplerenone. Although CYP3A4 is the primary metabolite of eplerenone, no active metabolites have been found in human plasma. Eplerenone, a white to almost white powder that belongs to class II of the BCS classification, is sparingly soluble in certain organic solvents and has a limited solubility in water. You can start with a recommended dose of 25 mg once daily and work your way up to 50 mg once daily[6].

MATERIAL AND METHODS:

Materials

Eplerenone was a complimentary sample provided by Dr. Reddy's Laboratories Ltd, Hyderabad. HPMC K4M, HPMC K15M, HPMC K100M, and Eudragit RSPO polymers were obtained as complementary samples from Glenmark Pharma, Nasik, India. Talc and magnesium stearate sourced from S.D. Fine Chemicals Pvt. Ltd, Mumbai, India. Lactose, PVP K30, and NaHCO3 were obtained from Signet Chemicals. All other ingredients utilized were of analytical grade and procured from SD Fine Chemicals Pvt Ltd, Mumbai, India.

Methods

Formulation of Eplerenone floating matrix tablets

Eplerenone floating matrix tablets were developed using the direct compression technique. The composition formulation of various batches is presented in Table 1. All the powders were filtered via a 40-mesh sieve. The requisite amount of Eplerenone, other polymers, and excipients was meticulously combined. Magnesium stearate and talc were ultimately incorporated as a lubricant and glidant, respectively. The dry blends were evaluated for several pre-compression parameters, including bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio. The assessed powder combination was directly compressed using 8 mm diameter, circular, flat-

faced punches on a 10-station rotating tablet punching machine. Each tablet comprised 25 milligrams of Eplerenone. All the tablets were preserved in sealed containers for subsequent analysis.

Table 1: Different Formulations of Eplerenone Floating Matrix Tablets

Formulations (mg)	EFT1	EFT2	EFT3	EFT4	EFT5	EFT6	EFT_7	EFT_8	EFT_9	EFT_{10}	EFT_{11}	EFT_{12}
Eplerenone	25	25	25	25	25	25	25	25	25	25	25	25
HPMC K4M	30	-	-	40	-	-	50	-	-	-	-	-
HPMC K15M	-	30	-	-	40	-	-	50	-	-	-	-
HPMC K100M	-	-	30	-	-	40	-	-	50	40	30	20
Eudragit RSPO	20	20	20	20	20	20	20	20	20	30	40	50
$NaHCO_3$	20	20	20	20	20	20	20	20	20	20	20	20
MCC	79	79	79	69	69	69	59	59	59	59	59	59
PVP K30	20	20	20	20	20	20	20	20	20	20	20	20
Mg. Stearate	4	4	4	4	4	4	4	4	4	4	4	4
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Total weight	200	200	200	200	200	200	200	200	200	200	200	200

Analytical Method for the *in vitro* Estimation of Eplerenone in the Formulations

Scanning: A sufficient concentration of 10 µg/ml was generated from the stock solution using a pH 1.2 hydrochloric acid buffer, followed by a UV scan conducted between 200-400 nm. The absorption maximum of 244 nm was selected for subsequent experiments.

Standard Plot: 100 mg of Eplerenone was precisely measured and placed into a 100 ml volumetric flask, then dissolved in a minimal volume of acidic buffer at pH 1.2. The volume was adjusted to 100 ml using an acidic buffer with a pH of 1.2 to achieve a concentration of 1000 µg/ml for stock solution I. One milliliter was extracted and diluted to 100 milliliters to achieve a concentration of 10 µg/ml for stock solution II. From the standard stock solution-II (SS-II), 1, 2, 3, 4, and 5 ml were extracted, and the total volume was adjusted to 10 ml using an acidic buffer at pH 1.2, resulting in concentrations of 1, 2, 3, 4, 5, 6, 8, and 10 µg/ml. The absorbance of these solutions was quantified relative to a blank at pH 1.2 and 244 nm for Eplerenone, with the results compiled in Table 4.1. A calibration curve was constructed, depicting drug concentrations in relation to absorbance[6].

Drug excipients compatibility studies:

FTIR study

A Fourier transform infrared (FTIR) analysis was conducted to ascertain any physical or chemical interactions between the pure medication and the polymers. FTIR analyses of the pure medication Eplerenone, HPMC K100M, ethyl cellulose, and the optimized formulation were conducted. The potassium bromide (KBr) pellet technique was employed. The pure medication was triturated with KBr, and a pellet was formed by applying a pressure of 100 kg/cm² for 2 minutes. The acquired pellet was evaluated using the FTIR 8400S instrument from Shimadzu, Japan. A KBr backdrop was acquired before the examination of the test samples. The identical process was reiterated for the analysis of the medication and its respective excipients[7].

DSC Studies

The differential scanning calorimetry (DSC) investigation of Eplerenone, HPMC K100M, and ethyl cellulose in the optimized formulation was conducted using a Shimadzu DSC 60 (Japan) to assess potential thermal interactions between the polymer and the medication. Samples weighing precisely 5 to 6 mg were hermetically sealed in an aluminum crucible and subjected to heating at a consistent rate of 10 °C/min across a temperature range of 40 to 300 °C. An inert environment was sustained by purging nitrogen gas at a flow rate of 50 ml/min [7].

Evaluation of pre-compression parameters of the dry powder blend of all formulations

Angle of Repose (θ):

This is the highest angle achievable between the surface of a powder pile and the horizontal plane. The powders were permitted to traverse through the funnel affixed to a stand at a specified height (h). The angle of repose was subsequently determined by measuring the height and radius of the granule heap[7].

$$\tan \theta = h/r$$

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

Where, θ = angle of repose
h = height of the heap
r = radius of the heap

According to the specifications, an angle of repose value less than 25^0 indicates excellent flow, whereas an angle between 25^0 and 30^0 indicates good flow. The angle between 30^0-40^0 indicates passable flow, and an angle greater than 40^0 indicates very poor flow [8].

Bulk density:
The loose bulk density (LBD) and tapped bulk density (TBD) were measured. Two grams of powder from each formula, previously agitated to disaggregate any produced agglomerates, were placed into a 10 ml measuring cylinder. After the observation of the initial volume, the cylinder was permitted to descend under its own weight onto a hard surface from a height of 2.5 cm at second intervals. The tapping persisted until no additional alteration in volume was seen. LBD and TBD were computed with the subsequent formulas[7].

$$LBD = \frac{weight\ of\ the\ powder}{volume\ of\ the\ packing}$$

$$TBD = \frac{weight\ of\ the\ powder}{tapped\ volume\ of\ the\ packing}$$

Compressibility Index (Carr's index):
The flowability of powder can be evaluated by comparing the loose bulk density (LBD) and tapped bulk density (TBD) of powder and the rate at which it is packed down.

Compressibility index (Carr's index) is calculated by the following formula

$$Carr's\ index\ (\%) = \frac{TBD-LBD}{TBD} \times 100$$

According to the specification, the Carr's index values between 5-15 indicate excellent flow, whereas between 12-16 indicate good flow. Values between 18-21 indicate fair-passable, whereas values between 23-25 indicate poor. Between 33-38 indicates very poor, and greater than 40 indicates extremely poor[9].

Hausner's ratio:

The Hausner's ratio of prepared Eplerenone floating tablets dry powder blends was determined by following the formula.

$$Hausner's\ ratio = \frac{TBD}{LBD}$$

According to specifications, values less than 1.25 indicate good flow (=20% of Carr's index), whereas values greater than 1.25 indicate poor flow (=33% of Carr's index). Between 1.25 and 1.5, adding glidant normally improves flow[9].

Content uniformity:
Two hundred milligrams of dry powder mixes, comprising an equivalent of 10 milligrams of Eplerenone, were dissolved in 100 milliliters of pH 1.2 HCl buffer and heated at 37°C for 15 to 20 minutes with stirring. The cooled solution was filtered using Whatman (no. 1) filter paper and thereafter measured spectrophotometrically at 244 nm following adequate dilution with pH 1.2 HCl buffer[10].

Evaluation of Eplerenone floating matrix tablets
Thickness
Ten Eplerenone floating tablets were randomly selected from each batch for thickness determination. The thickness of each tablet was assessed using a digital Vernier Calliper (Mitutoyo dial Thickness Gauge, Mitutoyo, Japan), and the results were presented as mean values of 10 measurements, accompanied by standard deviations[11].

Tablet Hardness
The Eplerenone floating tablets' hardness was measured by using the Monsanto hardness tester. From each batch, the crushing strength of ten floating tablets with known weights was recorded in $kg/cm^{2,}$ and the average was calculated and presented with standard deviation [13].

Friability
Initially, 10 tablets from each batch were subjected to testing in a Roche friabilator (Roche friabilator, Pharma Labs, Ahmedabad, India). The friabilator tablets were retrieved following 100 revolutions. The tablets were subsequently cleaned of dust, and the total remaining weight was documented. Friability was determined using the subsequent formula[14].
Percentage friability = (Initial weight – Final weight)/ Initial weight × 100

Weight variation test
All formed Eplerenone floating tablets were assessed for weight variation in accordance with the USP standard. Twenty pills were weighed both collectively and individually utilizing an electronic balance. The mean weight was determined, and the percentage variance of each tablet was computed[15,16].

Content uniformity
Twenty tablets were triturated, and an amount corresponding to one tablet was dissolved in 100

mL of pH 1.2 hydrochloric acid buffer. The solution was filtered, appropriately diluted, and the Eplerenone concentration was quantified using a UV Spectrophotometer (Elico, India) at 244 nm. Each measurement was conducted in triplicate, and the mean drug content in the floating tablet was determined[17, 18].

***In Vitro* Buoyancy Test**

The formulated floating tablets underwent an in vitro buoyancy assessment by being immersed in a 250 ml beaker filled with 200 ml of pH 1.2 HCl buffer at a temperature of 37±0.5 °C. The length for the tablet to ascend to the surface for flotation was designated as the floating lag time, while the floating duration of all tablets was assessed through visual inspection[19, 20].

***In Vitro* Drug Release**

In vitro drug release investigations were conducted utilizing the USP XXII dissolving equipment type II (Lab India DS 8000, Mumbai, India) at 37 ± 0.5ºC. The experiments were conducted at a rotating speed of 50 rpm, utilizing 900 ml of a pH 1.2 HCl buffer as the dissolution medium. 5 ml of the samples were extracted at one-hour intervals and substituted with an equivalent volume of buffer. The release of Eplerenone at various time intervals was quantified using an ultraviolet-visible spectrophotometer (Analytical Technology Ltd, Spectro 2080) at 244 nm following appropriate dilution. The trial was conducted in duplicate[21, 22].

Swelling index study

The degree of swelling was quantified as a percentage increase in the tablet's weight. The swelling index of all formulations was analyzed. One pill from each batch was placed in a Petri plate with a pH 1.2 hydrochloric acid buffer. The pill was extracted at two-hour intervals for a total duration of 12 hours, and surplus water was meticulously absorbed with filter paper. The swelling tablets were re-measured (Wt). The swelling index (SI) for each pill was determined using the subsequent equation [23,24].

$S.I. = \{(Wt-W0) / W0\} \times 100$

Where W_0 = initial weight, W_t = final weight

Characterization of the drug release profile

The release rate and mechanism of Eplerenone from the formulated floating matrix tablets were evaluated by fitting the dissolving data to certain exponential equations[25].

Zero-order release equation:

$$Q = K_0 t$$

Where Q is the amount of drug released at time t, and K_0 is the zero-order release rate constant.

The first order equation:

$$\ln (100 - Q) = \ln 100 - K_1 t$$

Where K_1 is the first-order release rate constant.

The dissolution data were fitted to Higuchi's equation:

$$Q = K_2 t^{1/2}$$

Where K_2 is the diffusion rate constant.

The dissolution data were also fitted to the Korsmeyer-Peppas equation, which is often used to describe the drug release behaviour from polymeric systems:

$$\text{Log } (Mt/M\infty) = \log K + n \log t$$

Where Mt is the amount of drug released at time *t*, M∞ is the amount of drug released after infinite time, K is a release rate constant, and n is the diffusion exponent indicative of the mechanism of drug release.

For matrix tablets, if the exponent $n < 0.5$, then the drug release mechanism is quasi-fickian diffusion (If $n = 0.5$, then fickian diffusion, and if the value is $0.5 < n < 1$, then it is anomalous diffusion coupled with erosion. An exponent value of 1 is indicative of Case-II Transport or typical zero-order and $n > 1$ non-Fickian super Case II. The diffusion exponent was based on the Korsmeyer-Peppas equation [26, 27].

RESULTS AND DISCUSSION:

Compatibility Studies

From the FTIR study, it was concluded that the peaks were found in the drug and polymers; the same peaks were found in the formulation, with negligible shifting peaks. It was confirmed that there is no interaction between the drug and polymers. Figure 1 shows the FTIR spectra of the medication as well as the formulations that were optimized.

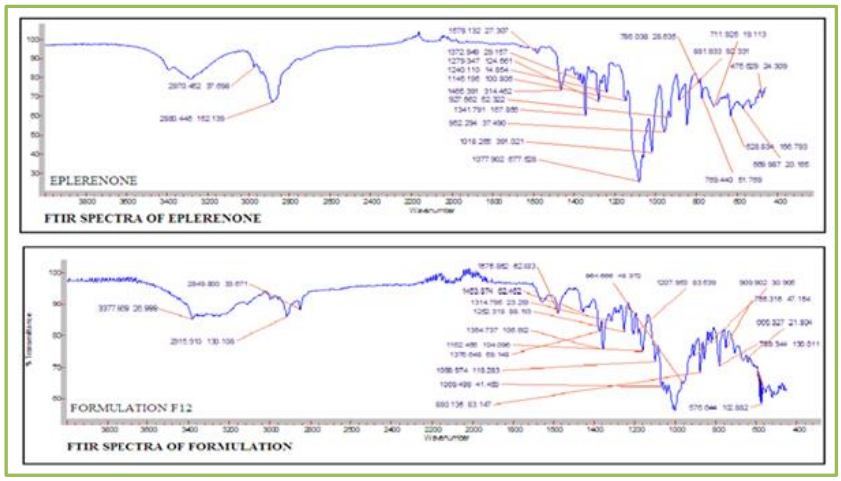

Fig. 1: FTIR spectra of Eplerenone floating matrix tablets

From the DSC thermograph, it was found that the melting point of pure drug was 219.2 °C, whereas in optimized formulation $EFT_{10,}$ the melting point was found to be 146.95 °C and 218.12 °C. So, it was confirmed that in the case of the DSC thermogram of EFT_{10}, the first endothermic peak at 146.95 °C was due to the drug, and the second peak at 218.12 °C was due to polymers. So, it was concluded that there is no significant drug and polymer interaction. The DSC thermograms of the medication and the optimized formulation are shown in Figure 2.

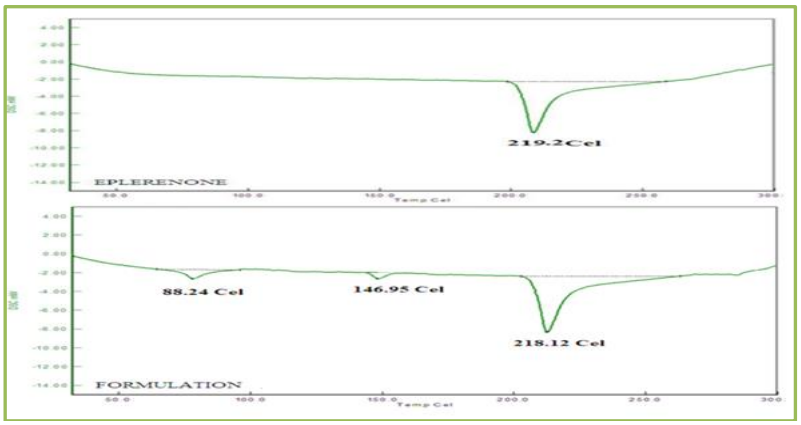

Fig. 2: DSC thermogram of Eplerenone floating matrix tablet

Pre-Compression Parameters

The tapped densities of dry powder blends of all formulations were found to be in the range of 0.280±0.01 to 0.330±0.02g/cm3, while the loose bulk densities of the blends were found to be in the range of 0.250±0.04 to 0.291±0.01g/cm3. This suggests that the granules have a high packing capacity. The measurements of bulk density and tapped density revealed that the density of a powder is dependent on the particle packing and that the density of the powder experiences a shift as it becomes more compact. In most cases, Carr's index values that are lower than 15% demonstrate favourable flow qualities, while readings that are higher than 25% suggest negative flowability. It was discovered that the range of Carr's index was between 09.24 and 14.08, which indicates excellent flow qualities. The Hausner ratio is a straightforward measure that may be used to assess the stability of a powder column and to speculate on the flow parameters. It was noticed that Hausner's ratio had a low range, which implies that they have a strong flow ability. It was discovered that Hausner's ratios of all formulations were between 1.10 and 1.16, which is typically indicative of adequate flow. When the particle is larger than 150µm, the angle of repose is used. An angle of repose with a value of 25 or less is often indicative of a material that flows freely, whereas an angle of 40 or more suggests that the material flows poorly. There is a correlation between the flowability of the material and the angle of repose observed. It can be concluded that the dry powder blends exhibited favourable flow qualities since the angle of repose of all formulations fell within the range of 20.3±0.10 to 22.6±0.10.

Table 2: Evaluation parameters of dry blends of Eplerenone floating matrix tablet (EFT_1- EFT_{12})

F. No.	Bulk density (g/cc)	Tapped density (g/cc)	Angle of repose (o)	Carr's index (%)	Hausner's ratio
EFT_1	0.272±0.02	0.313±0.03	21.2±0.12	13.09	1.15
EFT_2	0.291±0.01	0.330±0.02	20.3±0.06	11.81	1.13
EFT_3	0.284±0.03	0.325±0.04	21.4±0.07	12.62	1.14
EFT_4	0.276±0.04	0.304±0.03	22.5±0.13	9.21	1.10
EFT_5	0.250±0.04	0.291±0.02	20.4±0.11	14.08	1.16
EFT_6	0.241±0.03	0.280±0.01	22.3±0.08	13.93	1.16
EFT_7	0.276±0.02	0.314±0.02	21.5±0.11	12.10	1.14
EFT_8	0.287±0.04	0.323±0.03	22.6±0.10	11.14	1.13
EFT_9	0.272±0.03	0.310±0.02	21.4±0.11	12.26	1.14
EFT_{10}	0.284±0.01	0.318±0.03	20.3±0.10	10.69	1.12
EFT_{11}	0.285±0.03	0.314±0.04	21.2±0.09	09.24	1.10
EFT_{12}	0.288±0.05	0.324±0.02	20.3±0.11	11.11	1.12

Post-Compression Parameters

It was determined that all of the formulations of Eplerenone floating matrix tablets produced good results in terms of their physical properties. There were no instances of the typical tablet flaws that were found, such as capping, chipping, or picking. It was observed that the tablets had a thickness that varied between 3.30±0.12 and 3.42±0.07 millimeters. In every batch, the thickness was consistent throughout. The variances in weight measurements for various formulations were found to range from 3.1±0.3 to 4.4±0.4%. Because the average % variation of all tablet formulations was found to be within the limit, it can be concluded that all formulations were successful in passing the test for uniformity of weight as required by the official authority. Every single formulation of Eplerenone floating matrix tablets had a hardness that varied from 5.0±0.1 kg/cm2 to 5.9±0.2kg/cm2, falling within the specified range. Each of the formulations exhibited a percentage of friability that varied from 0.47±0.04% to 0.64±0.04%. Furthermore, it was observed that the percentage of friability rose as the quantity of sodium bicarbonate also increased. According to the findings of this investigation, the percentage of friability for all formulations was found to be within the limitations that were specified.

Table 3: Evaluation of post-compression parameters of Eplerenone floating matrix tablets (EFT_1- EFT_{12})

F. No.	Average hardness (kg/cm^2)	Percentage Weight Variation	Average friability (% w/w)	Average thickness (mm)
EFT_1	5.2±0.1	3.2±0.2	0.61±0.05	3.30±0.12
EFT_2	5.6±0.2	4.3±0.4	0.53±0.06	3.41±0.05
EFT_3	5.9±0.2	3.1±0.3	0.47±0.04	3.30±0.04
EFT_4	5.0±0.1	3.3±0.2	0.64±0.04	3.40±0.06
EFT_5	5.1±0.5	4.2±0.4	0.58±0.05	3.41±0.06
EFT_6	5.4±0.7	4.2±0.2	0.49±0.03	3.42±0.07
EFT_7	5.1±0.1	3.3±0.4	0.70±0.04	3.40±0.06
EFT_8	5.3±0.2	4.4±0.3	0.62±0.05	3.31±0.05
EFT_9	5.7±0.6	4.1±0.2	0.51±0.04	3.40±0.06
EFT_{10}	5.2±0.1	4.3±0.3	0.57±0.05	3.32±0.06
EFT_{11}	5.5±0.2	4.4±0.4	0.55±0.03	3.41±0.07
EFT_{12}	5.4±0.7	3.5±0.5	0.50±0.04	3.40±0.05

All values are expressed as mean± SD; (n=3)

Table 4: Evaluation of post-compression parameters of Eplerenone floating matrix tablets (EFT_1- EFT_{12})

F. No.	Content uniformity (%)	Floating lag time (sec)	Floating durations (hours)
EFT_1	99.36±1.1	46±0.2	10±0.2
EFT_2	100.48±1.0	34±0.1	11±0.1
EFT_3	99.66±1.1	30±0.3	12±0.2
EFT_4	98.28±1.2	48±0.2	10±0.2
EFT_5	99.54±1.1	35±0.2	11±0.1
EFT_6	99.69±1.2	27±0.1	12±0.2
EFT_7	99.85±1.2	47±0.2	11±0.1
EFT_8	98.78±1.1	39±0.2	12±0.2
EFT_9	99.74±1.0	31±0.3	13±0.1
EFT_{10}	99.85±1.2	28±0.2	14±0.3
EFT_{11}	99.48±1.0	27±0.4	13±0.4
EFT_{12}	99.62±1.1	26±0.1	14±0.4

All values are expressed as mean± SD; (n=3)

Uniformity of Content is a pharmaceutical analytical criterion for the quality control of capsules or tablets. The drug content percentages for Eplerenone floating matrix tablet formulations EFT_1 to EFT_{12} were found to vary from 98.28±1.2 to 100.48±1.0, within the permissible limits. The percentages were verified to be within the allowed range. The use of sodium bicarbonate, a gas-generating agent, resulted in all batches of floating tablets demonstrating significantly reduced floating lag times. All formulations had a floating lag time of under sixty seconds, which diminished with the increasing concentration of polymers. The duration of buoyancy is crucial for maintaining the formulation's suspension in stomach fluid. The floating duration for all formulations varies between 10 hours and 14 hours. An increase in polymer concentration correlates with an extended period of flotation observed. The maximum floating duration is indicated for EFT_{10} formulations.

***In Vitro* Drug Release Studies**

To optimize the in vitro drug release of Eplerenone floating matrix tablets, a variety of hydrophilic matrix polymers, including HPMC K4M, HPMC K15M, and HPMC K100M, as well as a hydrophobic matrix polymer, namely Eudragit RSPO, were used, and a total of twelve distinct formulations were created. When compared to the other two grades of HPMC that were used, the controlled release profile of HPMC K100M was much superior to that of the other two grades. Increasing the concentration of HPMC results in an increase in the impact of prolonging the release of the substance, and the optimal concentration of HPMC polymer was discovered to be 25%. It has been discovered that the use of HPMC polymer alone results in initial burst release due to the hydrophilic nature of the medication, and that the maximal release may continue for up to ten hours. To lessen the first burst release, however, an additional hydrophobic polymer, namely Eudragit RSPO, was included in the mixture. Because the initial release was 10% and the maximum release lasted for up to 12 hours, the EFT_{10} formulation that comprised 20% of HPMC K100M and 15% of Eudragit RSPO was determined to be an optimized formulation. When the concentration of Eudragit RSPO was increased even more, the initial release rate became much slower, which was not something that was desired. Therefore, a concentration of 15% Eudragit RSPO was deemed to be optimal. In Figure 3, the drug release profiles of several formulations were shown for comparison.

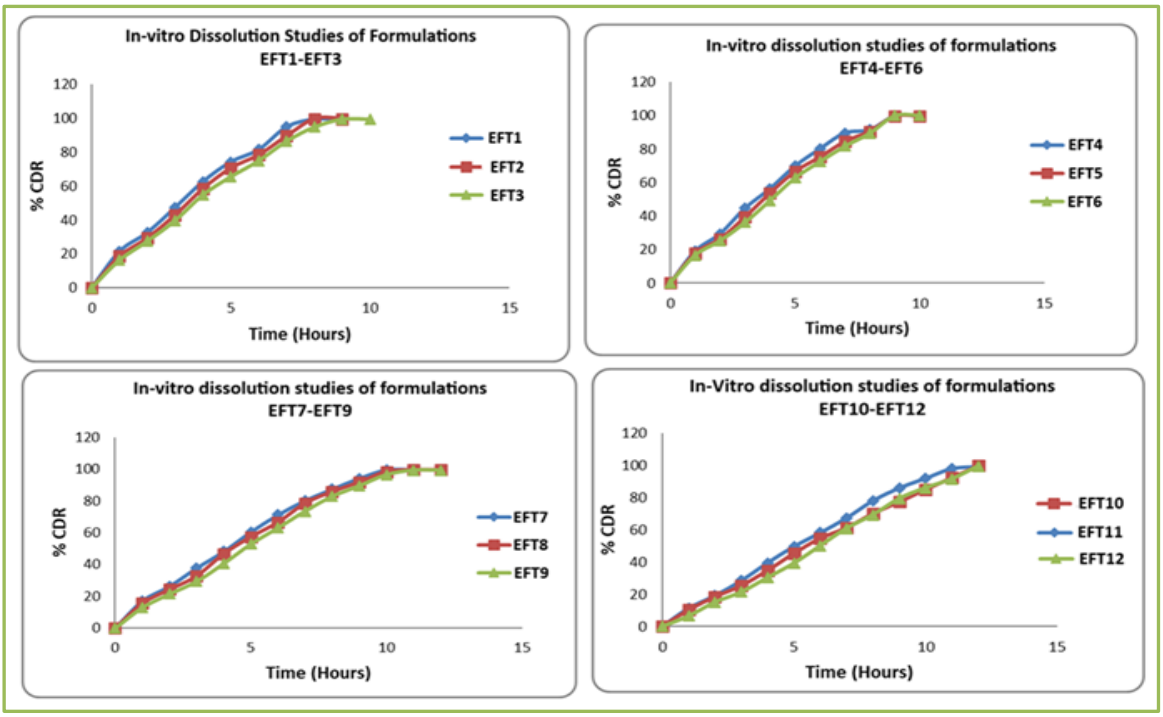

Fig. 3: *In vitro* dissolution studies

***In Vitro* Drug Release Kinetic Studies**

The results from the in vitro dissolution were fitted into a variety of kinetic models, including zero order, first order, Higuchi, and Korsmeyer-Peppas equations. As a result of the high regression values for the EFT10 formulation, it was discovered that the zero-order plots were rather linear. It was discovered that the release exponent 'n' for the optimized formulation EFT10 was 0.9241 ($0.5 < n < 1$), which seems to imply a link between the diffusion and erosion process, anomalous diffusion. Therefore, in the current investigation, the in vitro drug release kinetics of the Eplerenone floating matrix tablet were found to match the zero-order kinetic models. The mechanism of drug release was found to be anomalous diffusion combined with erosion.

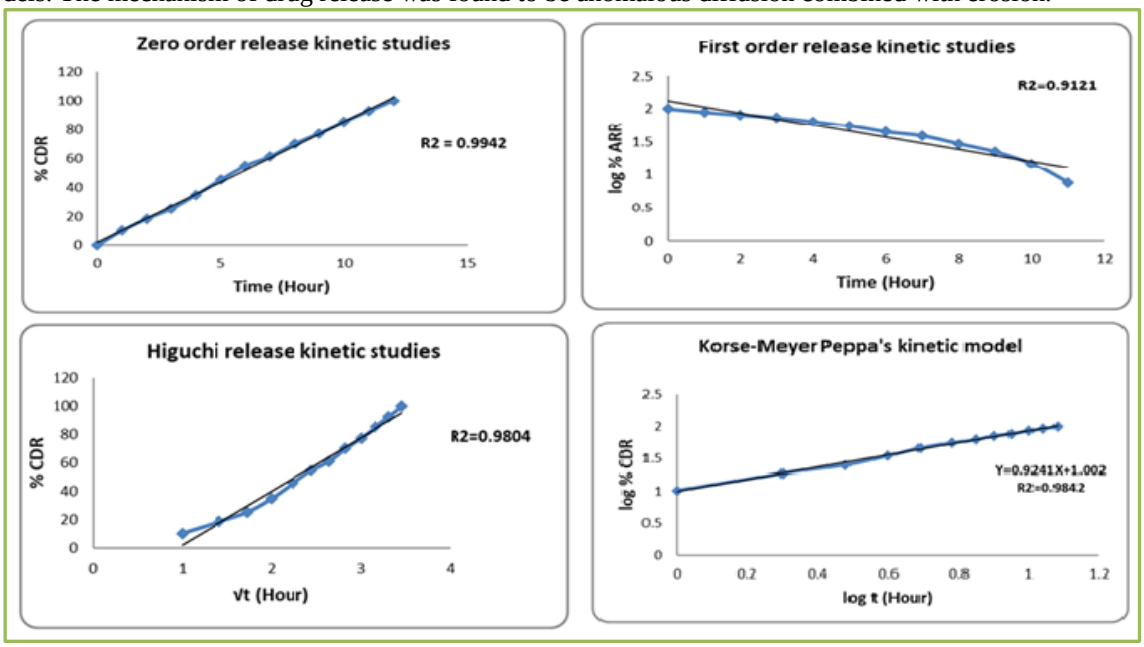

Fig. 4: Kinetic plot of Eplerenone floating tablet

CONCLUSION:

The present work successfully developed Eplerenone floating matrix tablets. The primary challenge of this study was assessing the influence of several low-density polymers on the in vitro release rate of floating Eplerenone tablets. A promising strategy for prolonging the drug's gastric residence time was floating delivery. A range of low-density matrix-forming polymers, such as Eudragit RSPO, HPMC K4M, HPMC K15M, and HPMC K100M, were examined. The main objective of integrating the hydrophobic polymer Eudragit RSPO with the hydrophilic polymer HPMC, which was successfully achieved, was to suppress the burst release phenomenon of the hydrophilic drug under examination. FTIR research indicated that the drug and polymers do not exhibit chemical interaction. DSC results indicated that the medication Eplerenone and the polymer employed in the present studies did not exhibit heat interaction. Various amounts of sodium bicarbonate were used as a gas-generating agent to enhance the tablet's buoyancy. The improved formulation, EFT10, comprising 15% Eudragit RSPO and 20% HPMC K100M, exhibited over 99% controlled drug release after 12 hours. The drug release profile exhibited a much slower rate with an increase in the concentration of both polymers. The enhanced formulation of EFT10 exhibited zero-order in vitro drug release kinetics, characterized by an anomalous diffusion and erosion release mechanism. In accordance with ICH requirements, stability studies were performed, demonstrating that the selected EFT10 formulation maintained stability for three months at 40°C and 75% relative humidity. In vitro floating studies indicated that the floating mechanism could prolong gastric residence time by as much as 12 hours, potentially enhancing the bioavailability of drugs that exhibit greater solubility in gastric fluids. Consequently, the outcomes of the current study indicate that the Eplerenone floating system holds significant promise as an alternative to conventional dosage forms.

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