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FORMULATION AND EVALUATION OF GASTRORETENTIVE EFFERVESCENT FLOATING TABLETS OF DILTIAZEM HCl

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ABSTRACT

In the present research work sustained release floating effervescent tablets of Diltiazem Hcl by using various concentrations of polymer were developed. The formulation blend was subjected to various preformualation studies, flow properties and all the formulations were found to be good indicating that the powder blend has good flow properties. Among all the formulations F8 formulation was retarded the drug release up to desired time period i.e., 12 hours in the concentration of 60 mg. The dissolution data of optimized formulation was subjected to release kinetics; from the release kinetics data it was evident that the formulation followed higuchi release kinetics.

KEYWORDS: Diltiazem HCl, Ethyl cellulose, Eudragit S-100, Eudragit L-100, effervescent floating tablets.

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. Over the last three decades, a various approaches have been pursued to prolong the residence time of a an oral dosage forms in the stomach, these methods include.

Floating drug Delivery Systems or Hydrodynamically Balanced Systems (HBS): These systems have a bulk density lower than gastric fluids and thus remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the systems are floating in the gastric contents, the drug is released slowly at a desired rate from the system. After the release of the drug, the residual system is emptied from the stomach. This results in an increase in the gastric retention time and a better control of fluctuations in

plasma drug concentration. HBS system contains a homogeneous mixture of drug and the hydrocolloid in a capsule, which upon contact with gastric fluid acquires a bulk density of less than 1 thereby being buoyant on the gastric contents of stomach until all the drug was released. Hydrodynamically balanced systems (HBS) are designed to prolong the stay of the dosage form in the gastro intestinal tract and aid in enhancing the absorption. Such systems are best suited for drugs having a better solubility in acidic environment and also for the drugs having specific site of absorption in the upper part of the small intestine. To remain in the stomach for a prolonged period of time the dosage form must have a bulk density of less than 1. It should stay in the stomach, maintain its structural integrity, and release drug constantly from the dosage form.

HBS system containing a homogeneous mixture of drug and the hydrocolloid in a capsule is developed, which upon contact with gastric fluid acquired and maintained a bulk density of less than 1 thereby being buoyant on the gastric contents of stomach until all the drug was released.

Based on the mechanism of buoyancy, two distinctly different technologies i.e., noneffervescent and effervescent systems have been utilized in the development of GFDDS.

Non-Effervescent GFDDS: The approach involved in the formulation of floating dosage forms is 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 one.

Effervescent GFDDS: The floating drug delivery systems utilize matrices prepared with swellable polymers such as methocel, polysaccharides, effervescent components like sodium bicarbonate, citric acid and tartaric acid or chambers containing a liquid that gasifies 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 gellyfied hydrocolloid. This produces an upward motion of the dosage form and maintains its buoyancy.

METHODOLOGY

MATERIALS

Table 1: List of Materials Used.

Name of the material	Source
Diltiazem HCl	Yarrow drug pvt ltd, Mumbai, India
Eudragit S-100	Merck Specialities Pvt Ltd, Mumbai, India
Eudragit L-100	Merck Specialities Pvt Ltd, Mumbai, India
Ethyl cellulose	Merck Specialities Pvt Ltd, Mumbai, India
Sodium bicarbonate	Merck Specialities Pvt Ltd, Mumbai, India
Magnesium stearate	Merck Specialities Pvt Ltd, Mumbai, India
Micro crystalline cellulose	Merck Specialities Pvt Ltd, Mumbai, India
Talc	Merck Specialities Pvt Ltd, Mumbai, India

Analytical method development

a) Determination of absorption maxima

A solution containing the concentration 10 µg/ ml drug was prepared in 0.1N HCl. UV spectrum was taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the range of 200 – 400.

b) Preparation calibration curve

100mg of Diltiazem HCl. Pure drug was dissolved in 100ml of 0.1NHcl (stock solution) 10ml of solution was taken and make up with100ml of 0.1N HCl (100µg/ml). The above solution was subsequently diluted with 0.1N HCl to obtain series of dilutions Containing 5, 10, 15, 20 and 25 µg/ml of Diltiazem Hcl per ml of solution. The absorbance of the above dilutions was measured at 236 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.

Drug – Excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy

The physical properties of the physical mixture were compared with those of plain drug. Samples was mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in Perkin Elmer IR spectrophotometer and the IR spectrum was recorded from 3500 cm to 500 cm. The resultant spectrum was compared for any spectrum changes.

Formulation development of Tablets

All the formulations were prepared by direct compression. The compressions of different formulations are given in Table. The tablets were prepared as per the procedure given below and aim is to prolong the release of Diltiazem HCl. Total weight of the tablet was considered as 300mg.

Procedure

1) Diltiazem HCl and all other ingredients were individually passed through sieve no □ 60.
2) All the ingredients were mixed thoroughly by triturating up to 15 min.
3) The powder mixture was lubricated with talc.
4) The tablets were prepared by using direct compression method.

Optimization of Sodium bicarbonate concentration

Sodium bicarbonate was employed as effervescent gas generating agent. It helps the formulation to float. Various concentrations of sodium bicarbonate were employed; floating lag time and floating duration were observed. Based on the concentration of sodium bicarbonate was finalized and preceded for further formulations.

Table 2: Optimization sodium bicarbonate concentration.

S.No	Excipient Name	EF1	EF2	EF3
1	Diltiazem (mg)	60	60	60
2	Eudragit S-100 (mg)	90	90	90
4	$NaHCO_3$(mg)	15	30	45
5	Mg.Stearate (mg)	3	3	3
5	Talc (mg)	3	3	3
7	MCC pH 102 (mg)	Q.S	Q.S	Q.S
8	Total weight (mg)	300	300	300

Table 3: Formulation composition for floating tablets.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Diltiazem HCl (mg)	60	60	60	60	60	60	60	60	60
Ethyl cellulose (mg)	30	60	90	-	-	-	-	-	-
Eudragit S-100 (mg)	-	-	-	30	60	90	-	-	-
Eudragit L-100 (mg)	-	-	-	-	-	-	30	60	90
$NaHCO_3$(mg)	45	45	45	45	45	45	45	45	45
Mag. Stearate (mg)	3	3	3	3	3	3	3	3	3
Talc (mg)	3	3	3	3	3	3	3	3	3
MCC pH102 (mg)	QS	QS	QS	QS	QS	QS	QS	QS	QS
Total weight (mg)	300	300	300	300	300	300	300	300	300

Evaluation of post compression parameters for prepared Tablets

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

Weight variation test

Twenty tablets were randomly selected and weighed, to estimate the average weight and that were compared with individual tablet weight. The percentage weight variation was calculated as per Indian Pharmacopoeial Specification. Tablets with an average weight 250 mg so the % deviation was ±5 %.

Table 4: IP standards of uniformity of weight.

S. No.	Average weight of tablet	% of deviation
1	≤ 80 mg	10
2	> 80 mg to <250 mg	7.5
3	≥ 250 mg	5

Friability test

Twenty tablets were weighed and subjected to drum of friability test apparatus. The drum rotated at a speed of 25 rpm. The friabilator was operated for 4 minutes and reweighed the tablets. % loss (F) was calculated by the following formula.

$F = 100 (W0-W)/W0$

Where W0 = Initial weight, W = Final weight

Hardness test

The hardness of tablets was measured by using Monsanto hardness tester. The results were complies with IP specification.

Thickness test

The rule of physical dimension of the tablets such as sizes and thickness is necessary for consumer acceptance and maintain tablet uniformity. The dimensional specifications were measured by using screw gauge. The thickness of the tablet is mostly related to the tablet hardness can be used as initial control parameter.

Drug content

The amount of drug in tablet was important for to monitor from tablet to tablet, and batch to batch is to evaluate for efficacy of tablets. For this test, take ten tablets from each batch were weighed and powdered. Weighed equivalent to the average weight of the tablet powder and

transferred into a 100 ml of volumetric flask and dissolved in a suitable quantity of media. The solution was made up to the mark and mixed well. Then filter the solution. A portion of the filtrate sample was analyzed by UV spectrophotometer.

***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).

***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, 9, 10, 11, 12
Temperature	--	37°C $\pm$ 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 $\pm$ 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 receptor fluid and analyzed by spectrophotometrically at 236 nm using UV-spectrophotometer.

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 are fitted to the following equation.

$$F = K_o t$$

Where, 'F' is the drug release at time't', and 'K_0' is the zero order release rate constant. The plot of % drug release versus time is linear.

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

$$\text{Log } (100\text{-}F) = kt$$

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then 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.

Korsmeyer and Peppas release model

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer- Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$$M_t / M_\infty = K t^n$$

Where, M_t / M_∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for super case II transport, n > 1. In this model, a plot of log (M^t / M^∞) versus log (time) is linear

RESULTS AND DISCUSSION

The present study was aimed to developing sustained release floating tablets of Diltiazem Hcl using synthetic polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release studies.

Analytical Method

Graph of Diltiazem HCl was taken in Simulated Gastric fluid (pH 1.2) at 236 nm.

Table 5: Observations for graph of Diltiazem HCl in 0.1N HCl (236 nm).

Conc [µg/ml]	Abs
0	0
5	0.128
10	0.272
15	0.393
20	0.543
25	0.692

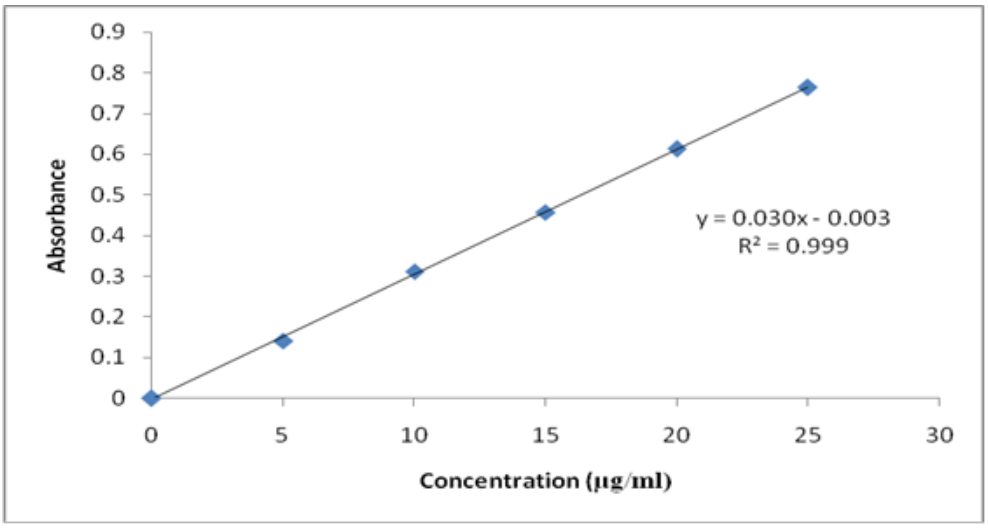

Figure 1: Standard graph of Diltiazem HCl in 0.1N HCl.

Drug – Excipient compatability studies

Fourier Transform-Infrared Spectroscopy

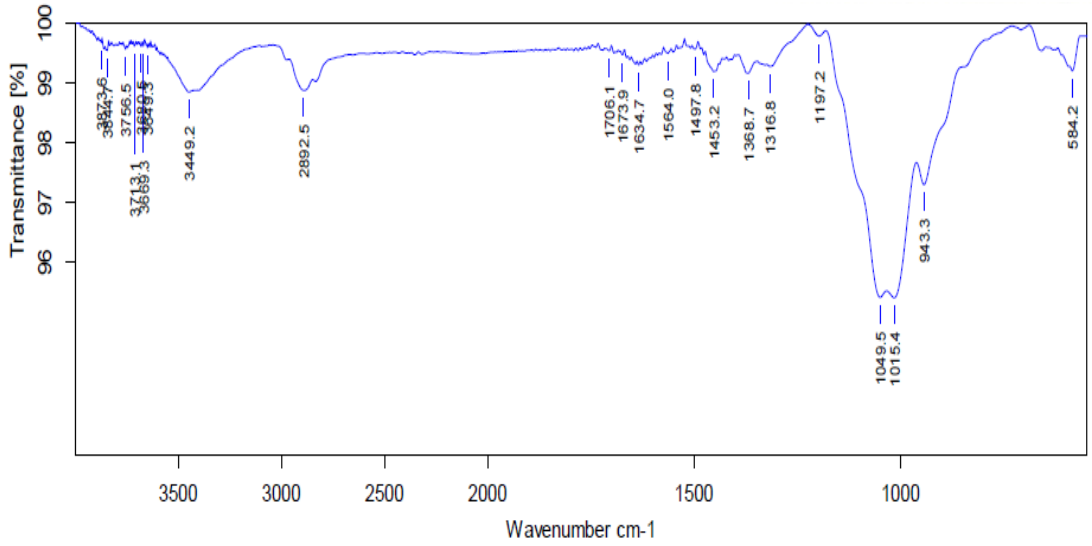

Figure 2: FT-TR Spectrum of Diltiazem HCl pure drug.

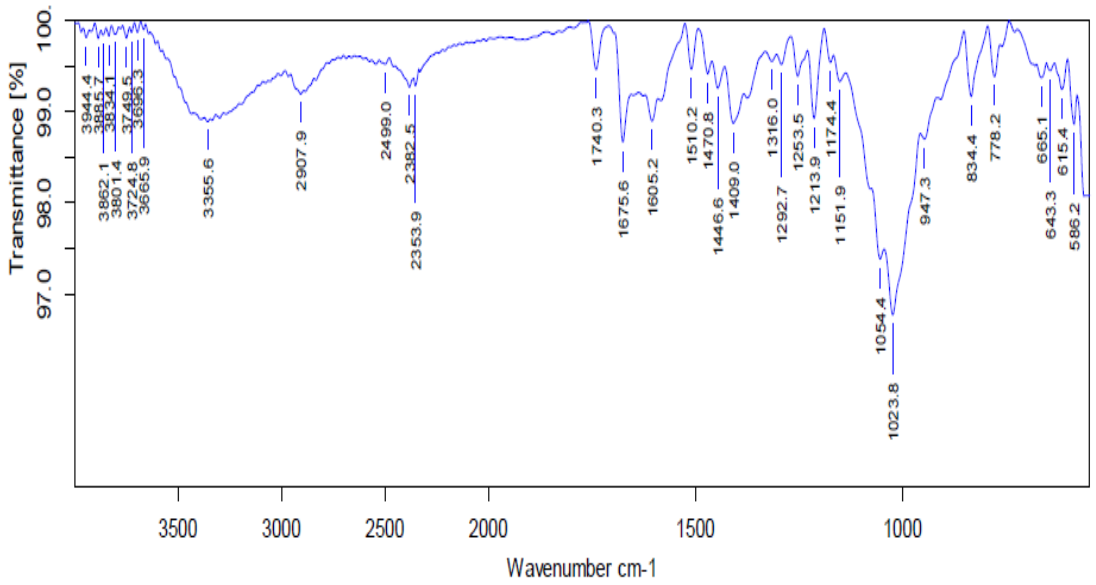

Figure 3: FT-IR Spectrum of Optimized Formulation(F8).

Fourier transform- Infrared spectrum of pure drug Diltiazem and optimized formulation were recorded on FT-IR Spectrophotometer and spectrum analysis was done for functional groups. Spectrum was checked for possible incompatibility. Peak values of optimized formulation and pure drug were found to be similar so there was no possible incomtibility between Drug and Excipients.

Table 6; comparission of FT-IR data of pure drug and optimized formulation.

Functional group	Aromatic CH Str	Ester C=O	Amide C=O	Aliphatic, C-H Stretch
6FI-IR value of pure drug	3449.2	1743.o4	1673.9	2892.5
FT-IR value Of optimized formulation	3355.6	1740.3	16756	2907.9

Preformulation parameters of powder blend

Table 7: Pre-formulation parameters of blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	27 ± 0.05	0.52 ± 0.04	0.61 ± 0.05	14.75 ± 0.04	1.17 ± 0.08
F2	25 ± 0.02	0.58 ± 0.05	0.64 ± 0.06	8.82 ± 0.06	1.10 ± 0.08
F3	29 ± 0.02	0.59 ± 0.05	0.66 ± 0.06	10.60 ± 0.04	1.11± 0.09
F4	25 ± 0.06	0.44 ± 0.08	0.52± 0.03	15.38 ± 0.05	1.18 ± 0.07
F5	26 ± 0.08	0.46 ± 0.06	0.53 ± 0.02	13.20 ± 0.05	1.15 ± 0.07
F6	26 ± 0.07	0.52 ± 0.07	0.60 ± 0.07	13.33 ± 0.04	1.15 ± 0.08
F7	28 ± 0.06	0.49 ± 0.06	0.56 ± 0.07	12.50 ± 0.06	1.14 ± 0.06
F8	28 ± 0.06	0.54 ± 0.06	0.61± 0.02	11.47 ± 0.03	1.12 ±0.06
F9	26 ± 0.12	0.58 ± 0.04	0.65 ± 0.02	10.76 ± 0.07	1.12 ± 0.04

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 0.44 ± 0.08 to 0.58 ± 0.05 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.52± 0.03 to 0.66 ± 0.06 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging from 8.82 ± 0.06 to 15.38 ± 0.05 which show that the powder has good flow properties. All the formulations have shown the hausner's ratio ranging from 0 to 1.25 indicating the powder has good flow properties.

Post compression Parameters For tablets

Tablet quality control tests such as weight variation, hardness and friability, thickness and drug release studies in different media were performed on the tablets.

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

Weight variation and thickness: All the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown in table 7.3. The average tablet weight of all the formulations was found to be between 298.4 ± 1.34 to 301.8 ± 0.75**.** The maximum allowed percentage weight variation for tablets weighing >250 mg is 5% and no formulations are not exceeding this limit. Thus all the formulations were found to comply with the standards given in I.P. And thickness of all the formulations was also complying with the standards that were found to be between 3.61 ± 0.01 to 3.91 ± 0.03.

Hardness and friability: All the formulations were evaluated for their hardness, using Monsanto hardness tester and the results are shown in table 7.3. The average hardness for all the formulations was found to be from 4.5 ± 0.14 to 4.8 ± 0.09 Kg/cm^2 which were found to be acceptable.

Friability was determined to estimate the ability of the tablets to withstand the abrasion during packing, handling and transporting. All the formulations were evaluated for their percentage friability using Roche friabilator and the results were shown in table. The average percentage friability for all the formulations was between 0.56 ± 0.08 and 0.66 ± 0.07, which was found to be within the limit.

Table 8: *In vitro* quality control parameters for tablets.

Formulation code	Weight variation (mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Flaoting lag time (min)	Duration of floating time (hr)
F1	298.5 ± 0.85	4.5 ± 0.14	0.56 ± 0.08	3.65 ± 0.03	99.11 ± 0.34	2.54 ± 0.01	8
F2	300.4 ± 0.43	4.7 ± 0.12	0.63 ± 0.05	3.84 ± 0.05	98.64 ± 0.51	2.33 ± 0.02	11
F3	299.7 ± 1.06	4.6 ± 0.13	0.58 ± 0.04	3.61 ± 0.01	99.44 ± 0.63	1.47 ± 0.01	12
F4	301.8 ± 0.75	4.7 ± 0.13	0.63 ± 0.08	3.82 ± 0.02	99.65 ± 0.43	2.32 ± 0.02	10
F5	299.3 ± 0.82	4.8 ± 0.09	0.57 ± 0.04	3.86 ± 0.03	99.34 ± 0.48	1.55 ± 0.01	10
F6	298.4 ± 1.34	4.6 ± 0.10	0.64 ± 0.09	3.74 ± 0.01	98.26 ± 0.53	1.88 ± 0.03	>12
F7	300.4 ± 0.73	4.7 ± 0.12	0.66 ± 0.07	3.78 ± 0.02	97.91 ± 0.41	1.44 ± 0.01	10
F8	298.6 ± 0.26	4.8 ± 0.08	0.58 ± 0.03	3.91 ± 0.03	99.52 ± 0.67	2.25 ± 0.02	12
F9	301.2 ± 0.43	4.7 ± 0.11	0.62 ± 0.06	3.81 ± 0.02	98.93 ± 0.34	1.42 ± 0.03	>1 2

Drug content: All the formulations were evaluated for drug content according to the procedure described in methodology section and the results were shown in table 7.3. The drug content Values for all the formulations were found to be in the range of **(**98.26 ± 0.53 to 99.52 ± 0.67**).** According to IP standards the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the formulations comply with the standards given in IP.

***In vitro* buoyancy studies:** All formulations were examined for buoyancy studies, in that to determine the floating lag time and duration of floating time. The floating lag time of most of the formulations were showed within 3mins. But duration of floating time was difference, it dependence on the concentration of polymer and type of polymer. Among all the formulation F3, F6, F8, F9 were showed 12 hours or more than 12 hours.

***In-Vitro* Drug Release Studies:** The in vitro dissolution studies were carried out by USP apparatus II (paddle) using pH 1.2 buffer and maintaining temperature 37 ± 0.5^0C, 50 RPM throughout period of dissolution (12 hours) test.

Table 9: Dissolution Data of Diltiazem Hcl Tablets Prepared With Ethyl cellulose in Different Concentrations.

TIME (hr)	CUMULATIVE PERCENT DRUG RELEASED (n=3 ± SD)		
	F1	F2	F3
0	0	0	0
0.5	34.57 ± 2.94	25.09 ± 1.36	16.98 ± 1.18
1	52.12 ± 1.61	34.45 ± 1.52	26.67 ± 1.24
2	70.45 ± 1.43	51.28 ± 1.66	37.35 ± 1.32
3	86.56 ± 2.73	68.31 ± 2.18	50.63 ± 1.29
4	99.48 ± 1.81	79.67 ± 1.46	67.45 ± 1.51
5	-	88.78 ± 2.37	76.43 ± 1.55
6	-	99.32 ± 1.29	89.63 ± 1.60
7	-	-	98.15 ± 2.37
8	-	-	-
9	-	-	-
10	-	-	-
11	-	-	-
12	-	-	-

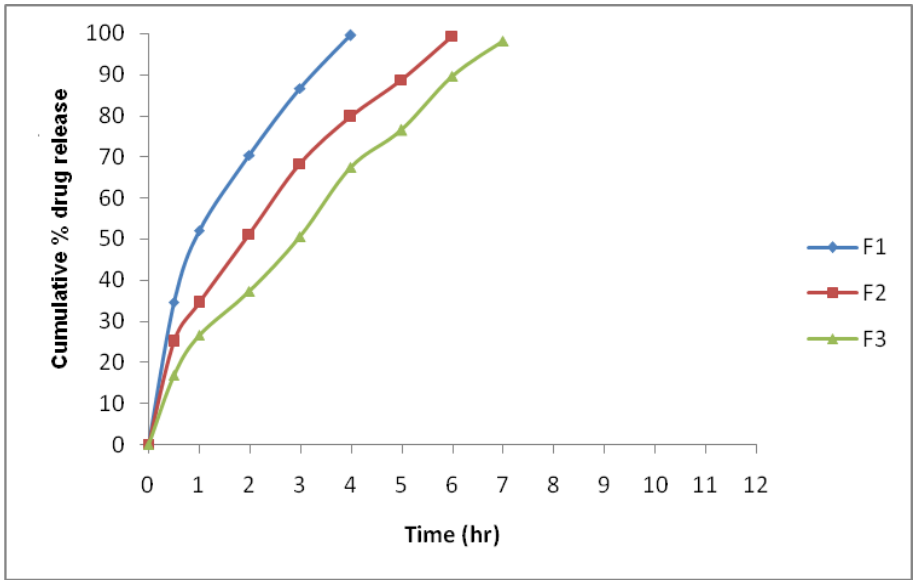

Fig 4: Dissolution profile of Diltiazem HCl floating tablets (F1, F2, F3 formulations).

From the dissolution data it was evident that the formulations prepared with ethyl cellulose was unable to retard the drug release up to desired time period.

Table 10: Dissolution Data of Diltiazem HCl Tablets Prepared With Eudragit S-100in Different Concentration.

TIME (hr)	CUMULATIVE PERCENT DRUG RELEASED (n=3±SD)		
	F4	F5	F6
0	0	0	0
0.5	30.21 ± 1.11	24.09 ± 1.98	15.61 ± 2.04
1	42.34 ± 1.45	32.12 ± 2.15	23.22 ± 1.55
2	63.22 ± 0.88	43.21 ± 0.95	30.81 ± 1.39
3	89.22 ± 1.55	55.18 ± 1.04	39.11 ± 2.16
4	99.15 ± 2.05	62.33 ± 1.42	46.15 ± 1.72
5	-	73.54 ± 1.71	53.16 ± 1.51
6	-	82.63 ± 1.44	60.21 ± 1.83
7	-	99.24 ± 1.96	66.25 ± 1.88
8	-	-	72.36 ± 1.53
9	-	-	78.28 ± 1.61
10	-	-	85.52 ± 2.02
11	-	-	92.45 ± 1.29
12	-	-	99.55 ± 1.55

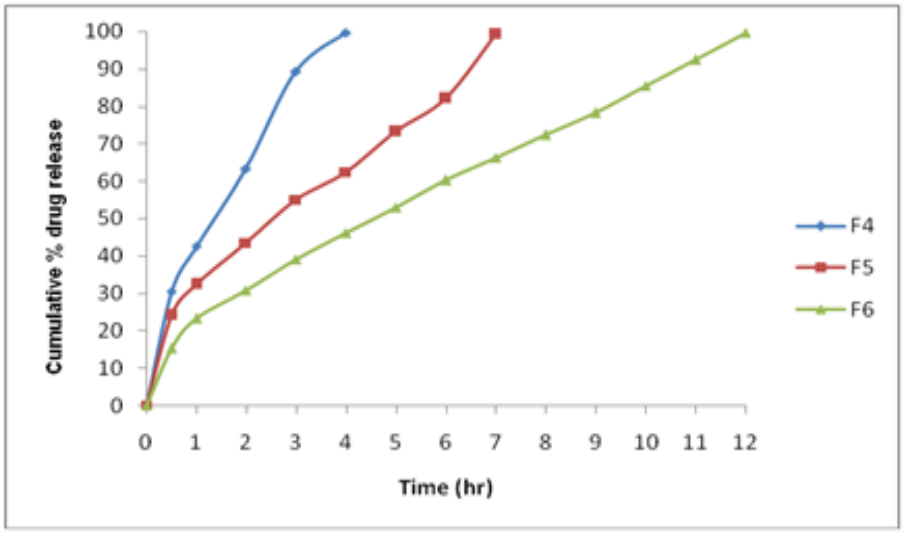

Fig 5: Dissolution profile of Diltiazem HCl floating tablets (F4, F5, F6 formulations).

The formulations prepared with Eudragit S-100 also unable to retard the drug release at lower concentration of polymer whenever increase the concentration of Eudragit S-100 in the formulation (F6) it was showed maximum drug release at 12 hours (i.e. . 99.55 ± 1.55).

Table 11: Dissolution Data of Diltiazem HCl tablets prepared with combination of Eudragit L-100 in Different Concentrations.

TIME (hr)	CUMULATIVE PERCENT DRUG RELEASED (n=3±SD)		
	F7	F8	F9
0	0	0	0
0.5	36.23 ± 1.58	24.61 ± 2.14	18.77 ± 1.24
1	49.42 ± 0.98	30.53 ± 1.85	25.91 ± 1.09
2	56.90 ± 1.26	36.84 ± 1.67	30.23 ± 1.85
3	65.56 ± 2.05	42.53 ± 2.05	35.13 ± 1.15
4	77.54 ± 1.46	49.76 ± 1.26	40.51 ± 1.38
5	83.56 ± 1.34	55.21 ± 1.86	46.67 ± 1.65
6	90.45 ± 1.25	60.25 ± 2.14	51.57 ± 2.11
7	99.67 ± 2.05	66.13 ± 1.34	58.69 ± 1.26
8	-	73.24 ± 2.18	65.67 ± 1.31
9	-	79.09 ± 1.64	69.22 ± 1.16
10	-	85.34 ± 1.85	76.32 ± 2.08
11	-	91.41 ± 2.14	81.39 ± 1.34
12	-	99.98 ± 1.08	87.21 ± 1.25

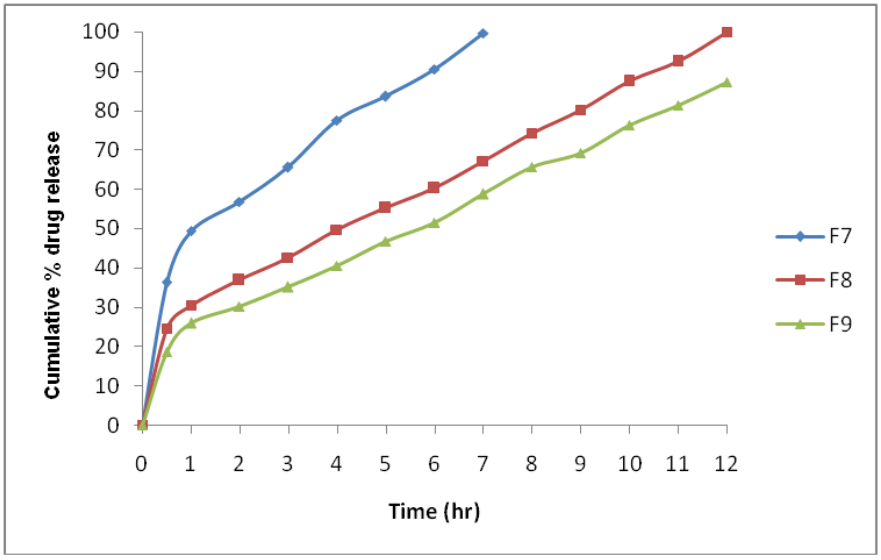

Fig 6: Dissolution profile of Diltiazem HCl floating tablets (F7, F8, F9 formulations).

The drug release of formulations prepared with combination of Eudragit L100 dependence on the concentration of polymer in the formulation. At low concentration, unable to retard the drug release whenever increase the concentration of polymer in formulation i.e. 60mg (F8) was showed maximum drug release up to 12 hours (i.e. 99.98 ± 1.08) and it was showed good floating lag time and duration of floating time. When increase the concentration of polymer to 90 mg it showed maximum drug release after 12 hours. So that formulation was not considered.

Among all the formulation, F8 formulation was considered as optimized formulation.

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.

Table 12: Release kinetics data for optimised formulation.

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN
0	0	0	-	-	2.000
24.61	0.5	0.707	1.391	-0.301	1.877
30.53	1	1.000	1.485	0.000	1.842
36.84	2	1.414	1.566	0.301	1.800
42.53	3	1.732	1.629	0.477	1.759
49.76	4	2.000	1.697	0.602	1.701
55.21	5	2.236	1.742	0.699	1.651
60.25	6	2.449	1.780	0.778	1.599
66.13	7	2.646	1.820	0.845	1.530
73.24	8	2.828	1.865	0.903	1.427
79.09	9	3.000	1.898	0.954	1.320
85.34	10	3.162	1.931	1.000	1.166
91.41	11	3.317	1.961	1.041	0.934
99.98	12	3.464	2.000	1.079	-1.699

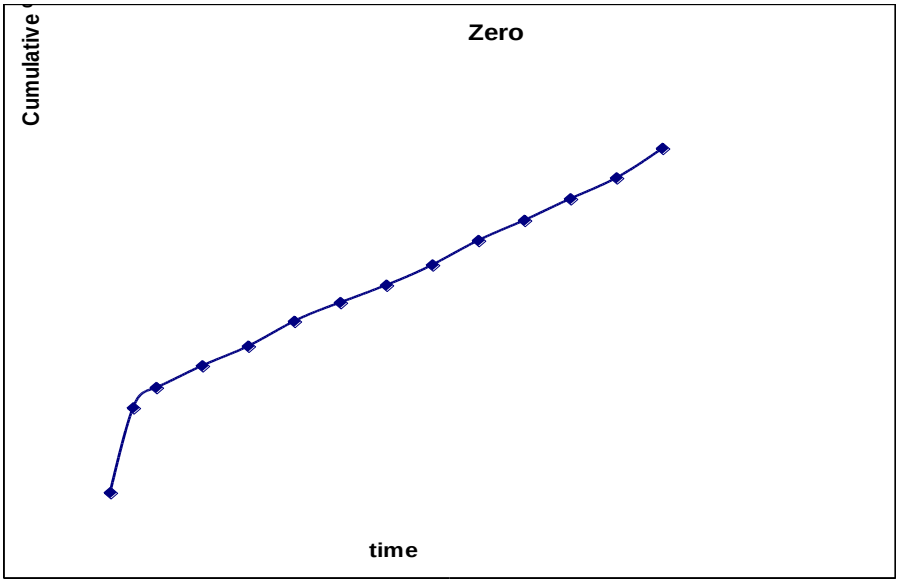

Fig 7.6: Zero order release kinetics graph.

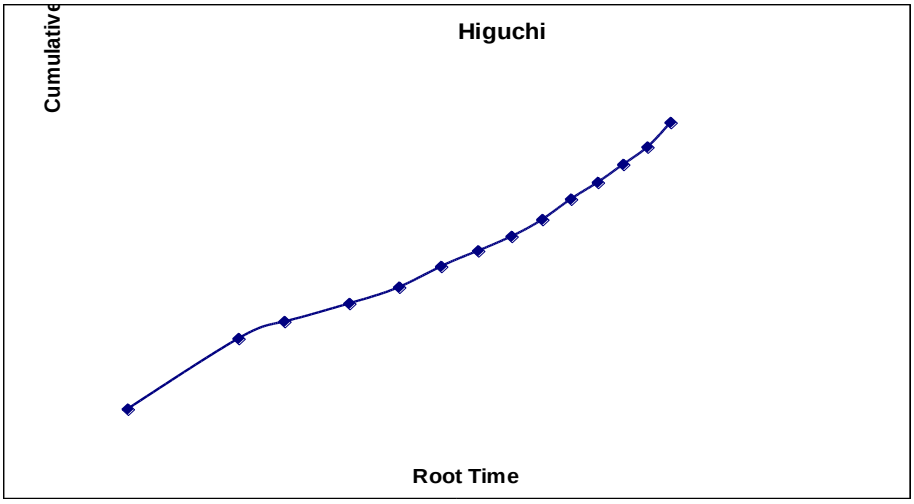

Fig 7: Higuchi release kinetics graph.

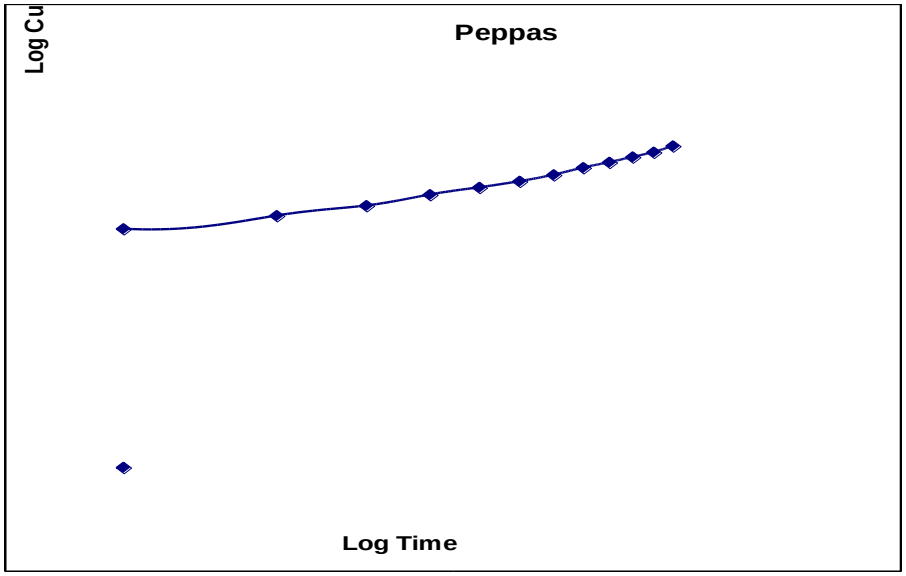

Fig 8: Kors Mayer peppas graph.

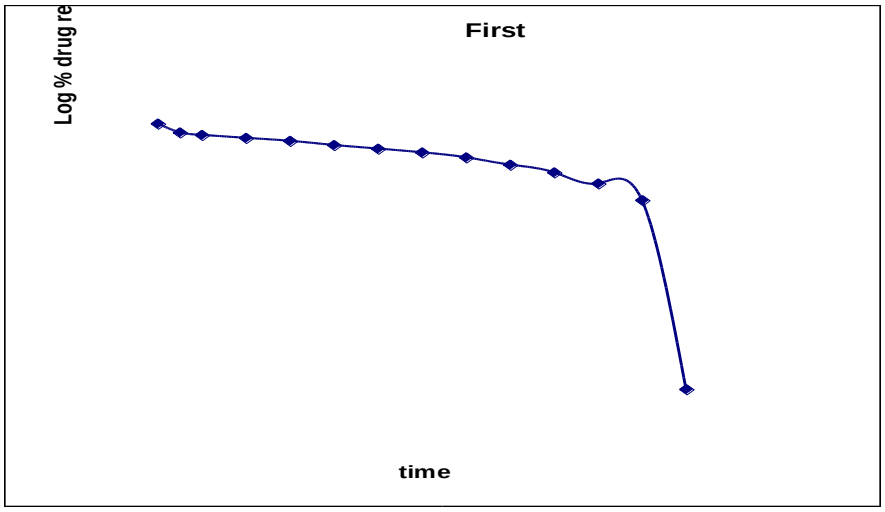

Fig 9: First order release kinetics graph.

From the above graphs it was evident that the formulation F8 was followed Higuchi release kinetics.

CONCLUSION

The present study concludes that sustained release floating tablets of Diltiazem HCl prepared by effervescent method and using different concentration of ethyl cellulose, Eudragit S-100 and Eudragit L100 as retarding polymers. Among all the formulations F6 and F8 formulations have shown optimised results. Preformulation data indicates all formulations have good flow properties. In vitro quality control parameters indicates all formulations comply with in the standards given in I.P. Based on dissolution profile and percentage drug release F8 Formulation showed maximum drug release up to 12 hours (99.98±1.08) and it was showed good floating log time and duration of floating time. FT-IR data of optimized formulation is similar to the pure drug so there is no interaction between drug and excipients. Applied release data kinetics indicates optimized formulation (F8) follows kors Mayer and Higuchi release kinetics. Regression coeffient value for Higuchi release kinetic graph is 0.979.This indicates the drug follows diffusion mechanism. Regression coefficient value for Kors-mayer and Peppas graph is 0.963. n value of optimized formulation was found to be 0.439 so it follows Diffusion controlled Fickian type of mechanism. Present study concludes that gastro retentive floating system may be a suitable method for Diltiazem HCl.

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