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Formulation and *In-Vitro* Evaluation of Gastroretentive Floating Tablets of Hydrochlorthiazide

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A B S T R A C T

In the present research work gastro retentive floating matrix formulation of Hydrochlorthiazide by using various hydrophilic polymers. Initially analytical method development was done for the drug molecule. Absorption maxima was determined based on that calibration curve was developed by using different concentrations. Gas generating agent sodium bicarbonate concentration was optimized. Then the formulation was developed by using different concentrations of polymers of various grades of HPMC and guar gum. The formulation blend was subjected to various pre-formulation 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 the formulations prepared by using Guar gum were unable to produce desired drug release, they were unable to retard drug release up to 12 hours. The formulations prepared with HPMC K 100 M retarded the drug release up to 12 hours in the concentration of 60 mg (F6).The formulations prepared with HPMC K15M were also retarded the drug release for more than 12 hours. Hence they were not considered. The optimized formulation dissolution data was subjected to release kinetics, from the release kinetics data it was evident that the formulation followed Higuchi mechanism of drug release.

Keywords: Hydrochlorthiazide, HPMC polymers, Floating tablets.

A R T I C L E I N F O

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1. Introduction

Oral Controlled Drug Delivery

Oral drug delivery has been the most widely utilized route of administration due to its ease of administration, low cost of therapy, improved patient compliance and as well as the traditional belief that, by oral administration the drug is as well absorbed as the foodstuffs that are digested daily. From immediate release to site-specific delivery, oral dosage forms have really progressed. However, it is a well-accepted fact that it is difficult to predict the real *in vivo* time of release with solid, oral controlled release dosage forms. Thus, drug absorption in the gastrointestinal tract (GIT) may be very short and highly variable in certain circumstances. The extent of GIT drug absorption is related to contact time with the mucosa.

Conventional dosage forms, including prolonged-release dosage forms, does not usually provide rate-controlled release or target specificity. Controlled drug delivery systems offer several advantages which has lead to intense advancements in the development in the new drug delivery system. Here are some of the reasons for the intense advancement in the new systems. First, recognition of the possibility of repeating successful drugs by applying concepts and techniques of controlled release drug delivery systems, coupled with increasing expense in bringing new drug entities to market, has encouraged the development of new drug delivery systems. Second, new systems are needed to deliver novel, genetically engineered pharmaceuticals, i.e., peptides and proteins, to their site of action without incurring significant immunogenicity. Third, treatment of enzyme deficient diseases and cancer therapies can be improved by better targeting.Finally, therapeutic efficacy and safety of drugs, administered by conventional methods, can be improved by more precise spatial and temporal placement within the body, thereby reducing both size and number of doses. In addition, DDS offer tremendous benefits to the innovator.

At present, no available drug delivery systems can achieve all these goals. In many cases, conventional drug delivery provides sharp increase of drug concentration at potentially toxic levels. Following a relatively short period at the therapeutic level, drug concentration eventually drops off until re-administration. While, rate controlled release drug delivery systems are capable of delivering a drug at predetermined rate either systematically or locally for a specific period of time, but they do so with virtually no control over the fate of the drug once it enters the body. Targeted drug delivery systems, on the other hand, while capable of achieving site specific delivery, are usually unable to control the release kinetics of drug in a predictable manner.

Advantages of long-acting controlled drug delivery systems

Some of the major advantages of the controlled drug delivery systems are as follows:-

- Controlled release drug administration means not only to prolong duration of drug delivery as in sustained release and prolonged release, but also implies predictability and reproducibility of drug release kinetics.
- Administration of drugs in conventional dosage forms often results in see-saw fluctuations of drug concentration in systematic circulation. A well-designed, controlled drug delivery system can significantly reduce the frequency of drug dosing and also maintain a steady drug concentration in blood circulation and target tissue cells.
- The pronounced fluctuations resulting from the conventional drug administration are likely to yield periods of no therapeutic effects when the drug concentration is below minimum effective dose level (MED) or adverse reactions take place when the drug concentration exceeds the toxic dose level.
- Drug concentration can be maintained within a narrow therapeutic range by the use of controlled release drug delivery systems which will also minimize the incidence and severity of adverse side effects.
- The controlled release drug delivery systems can be designed to release drugs in the vicinity of the target tissues that require treatment while the drug exposure of other non-target tissue is minimized.
- The therapeutic effectiveness of the drug, that is the overall pharmacological response per unit dose, can be enhanced by choosing the optimal drug delivery rate, the rate that yields the most effective drug concentration in the target tissue cells. Thus the use of controlled release drug delivery systems maximizes the bioavailability.

Disadvantages of long-acting controlled drug delivery systems

There are several potential disadvantages of controlled release formulations. Some of them are as follows:

a. *In vitro In vivo* correlations for controlled release dosages are very poor in which rate release over greater regions of gastrointestinal tract with potential reduction in systemic availability. There is no reason to suspect that *in vitro - in vivo* correlations would not be worse.
b. Dose dumping is a phenomenon whereby relatively large quantity of medication in a controlled release formulation is rapidly released, introducing potential toxic quantities of drug into the systemic circulation. However, dose dumping should not be a problem with good manufacturing practice and the types of rigid controls that have become standard in the industry.
c. Reduced potential for dosage adjustment is a major disadvantage of some controlled release products. This should be considered when preparing controlled release formulations for drugs that are available in a variety of strengths in conventional dosages. The controlled release formulation should also be available in a variety of strengths or in a form that can easily be subdivided without losing controlled release properties.

d. The potential for reduced drug absorption is other disadvantage of controlled release formulation as it causes a fraction of administered drug to be released in the regions of the gastrointestinal tract that are distal to the optimum absorptive region of the small intestine. The so called "absorption window" becomes important and this may give rise to unsatisfactory drug absorption in-vivo despite excellent release characteristics *in vitro*.

The high cost of controlled release dosage forms must also be taken into account while development of such products. Several formulation parameters can affect the gastric residence time. More reliable gastric emptying patterns are observed for multi-particulate formulations as compared with single unit formulations, which suffer from "all or none concept." As the units of multi-particulate systems are distributed freely throughout the gastrointestinal tract, their transport is affected to a lesser extent by the transit time of food compared with single unit formulation (Bechgaard and Ladefoged, 1978).

Classification of floating drug delivery systems

1. Single unit floating drug delivery systems
   - Non-effervescent systems
   - Effervescent (gas generating) systems
2. Multiple unit floating drug delivery systems
   - Non-effervescent systems
   - Effervescent (gas generating) systems
   - Hollow microsphere
3. Raft forming systems

Single unit floating drug delivery systems

Depending upon the mechanism of floating, there are two types of single unit systems, non-effervescent and effervescent.

Non-effervescent *systems*

These systems usually contain one or more type of swell-able cellulose type of hydrocolloids, polysaccharides, and matrix-forming polymers like polycarbonate, polyacrylate, polymethacrylate, and polystyrene. The formulation method includes a simple approach of thoroughly mixing the drug and the gel-forming hydrocolloid. After oral administration this dosage form swells in contact with gastric fluid and attains a bulk density of <1. After coming into contact with gastric fluid, these gel formers, polysaccharides, and polymers hydrate and form a colloidal gel barrier that controls the rate of fluid penetration into the device and consequent drug release from gelatinous mass. As the exterior surface of the dosage form dissolves, the gel layer is maintained by the hydration of the adjacent hydrocolloid layer. The air trapped by the swollen polymer lowers the density and confers buoyancy to the dosage form.

Effervescent systems

These kinds of buoyant delivery systems are prepared with swell-able polymers or polysaccharides e.g.- HPMC and effervescent components, e.g.- sodium bicarbonate and citric or tartaric acid (Rubinstein and Friend, 1994)or matrices containing chambers of liquid that gasify at body temperature (**Ritschel, 1991**). The matrices are fabricated so that upon contact with gastric fluid, carbon dioxide is librated by the acidity of gastric contents and is entrapped in the matrix of 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 layer and the drug in the other layer formulated for the sustained release effect.

2. Materials and Method

Materials:

Hydrochlorthiazide, different grades of HPMC polymers, Guar gum, Sodium bicarbonate, Magnesium stearate, Micro crystalline cellulose, Talc.

Analytical method development:

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.

Preparation calibration curve:

100 mg of Hydrochlor-thiazide pure drug was dissolved in 100 ml of water(stock solution) 10 ml of solution was taken and make up with 100 ml of water (100 µg/ml).from this 10 ml was taken and make up with 100 ml of water (10 µg/ml). The above solution was subsequently diluted with 0.1N HCl to obtain series of dilutions Containing 2,4,6,8,10, 20,30,40,50,60, 70, 80, 90 and 100 µg/ml of Hydrochlorthiazide per ml of solution. The absorbance of the above dilutions was measured at 271 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.

Pre-formulation parameters

The quality of tablet, once formulated by rule, is generally dictated by the quality 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.

Angle of repose:

The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel.

Bulk density:

Density is defined as weight per unit volume. Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a

powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting.

Tapped density:

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit.

Measures of powder compressibility:

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flow-able it is. As such, it is measures of the relative importance of inter-particulate interactions. In a free- flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value.

Formulation development of Tablets:

All the formulations were prepared by direct compression. The compression of different formulations are given in Table 6.3. The tablets were prepared as per the procedure given below and aim is to prolong the release of Hydrochlorthiazide Hydrochloride. Total weight of the tablet was considered as 300 mg.

Procedure:

a. Hydrochlorthiazide and all other ingredients were individually passed through sieve no ≠ 60.
b. All the ingredients were mixed thoroughly by triturating up to 15 min.
c. The powder mixture was lubricated with talc.
d. 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 that the concentration of sodium bicarbonate was finalized and preceded for further formulations.

Table 1: Optimization sodium bicarbonate concentration

S. No	Excipient Name	EF1	EF2	EF3
1	Hydrochlorthiazide	12.5	12.5	12.5
2	HPMC K 100M	20	40	60
4	$NaHCO_3$	20	20	20
5	Mg.Stearate	3	3	5
6	Talc	3	3	3
7	MCC pH 102	Q.S	Q.S	Q.S

All the quantities were in mg.

Based on the floating lag time and floating duration the concentration of sodium bicarbonate was optimised.

Evaluation of post compression parameters for prepared Tablets

The designed formulation compression coated 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 weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation 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.

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).

In vitro Buoyancy studies:

The in vitro buoyancy was determined by floating lag time, and total floating time. (As per the method described by Rosa et al) The tablets were placed in a 100 ml 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 -- 75
Sampling intervals (hrs) -- 0.5,1,2,3,4,5,6,7,8,10,11,12
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:

900 ml of 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 75 rpm. At definite time intervals of 5 ml of the receptors fluid was withdrawn, filtered and again 5 ml receptor fluid was replaced. Suitable dilutions were done with receptor fluid and analyzed by spectro-photometrically at 271 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_o' 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

$$Log (100-F) = kt$$

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 supercase II transport, n > 1. In this model, a plot of log (M_t/ M_∞) versus log (time) is linear.

Hixson-Crowell release model:

Hixson-Crowell model describes the release of drugs from an insoluble matrix through mainly erosion. (Where there is a change in surface area and diameter of particles or tablets).

3. Results and Discussion

The present study was aimed to developing gastro retentive floating tablets of Hydrochlorthiazide using various HPMC polymers. All the formulations were evaluated for physicochemical properties and *in-vitro* drug release studies.

Analytical Method: Graphs of Hydrochlorthiazide was taken in Simulated Gastric fluid (pH 1.2) at 271 nm.

Table 2: Observations for graph of Hydrochlorthiazide in 0.1N HCl (271 nm)

Conc [µg/l]	Abs
2	0.013
4	0.024
6	0.034
8	0.043
10	0.055
15	0.078
20	0.103
30	0.158
40	0.205
50	0.257
60	0.302
70	0.358
80	0.411
90	0.456
100	0.503

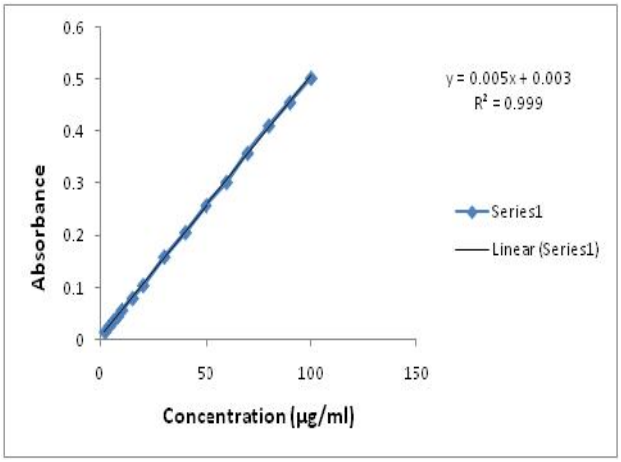

Figure 1: Standard graph of Hydrochlorthiazide in 0.1N HCl

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 0.43±0.07 to 0.58±0.06 (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 0.57 to 0.69 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging between 16 to 18 which shows that the powder has good flow properties. All the formulations has shown the hausner ratio ranging between 0 to 1.2 indicating the powder has good flow properties.

Optimization of sodium bicarbonate concentration:

Three formulations were prepared with varying concentrations of sodium bicarbonate. The formulation containing sodium bicarbonate in 20 mg concentration

showed less floating lag time of 4 min and the tablet was in floating condition for more than 12 hours.

Quality Control 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.

***In-vitro* quality control parameters for tablets**

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

***In-Vitro* Drug Release Studies**

Table 3: Dissolution Data of Hydrochlorthiazide Tablets Prepared with Guar gum In Different Concentrations

Time **(hr)**	**Cumulative percent drug dissolved (n=3±sd)**		
	F1	**F2**	**F3**
0.5	21.73	18.52	19.53
1	59.23	37.47	28.97
2	84.9	59.93	35.89
3	94.873	65.85	45.7
4	94.873	77.54	54.38
5		89.55	61.2
6		96.6	67.06
7			72.52
8			77.88
9			86.6
10			89.09
11			94.52

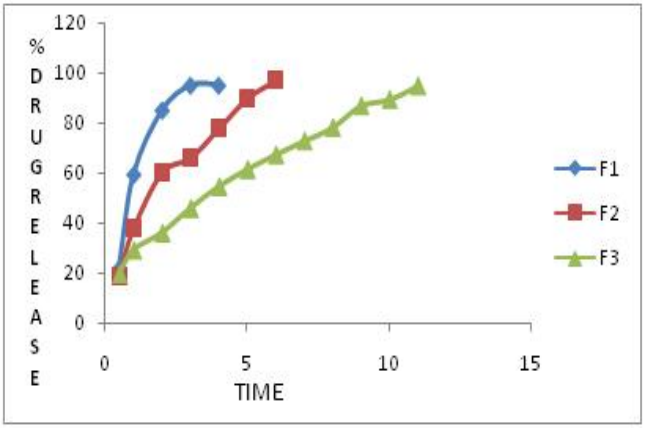

Figure 2: Dissolution profile of Hydrochlorthiazide HCl floating tablets (F1, F2, F3 formulations).

Table 4: Dissolution Data of Hydrochlorthiazide Tablets Prepared With HPMCK15M in Different Concentrations

Time **(hr)**	**Cumulative percent drug dissolved (n=3±sd)**		
	F4	**F5**	**F6**
0.5	18.45	18.42	19.62
1	36.26	27.73	27.86
2	52.16	35.63	36.35
3	70.01	42.04	41.45
4	87.26	57.25	47.80
5	93.10	64.33	55.25
6		75.41	60.24
7		83.84	66.73
8		92.80	71.34
9			78.52
10			80.17
11			88.75
12			96.33

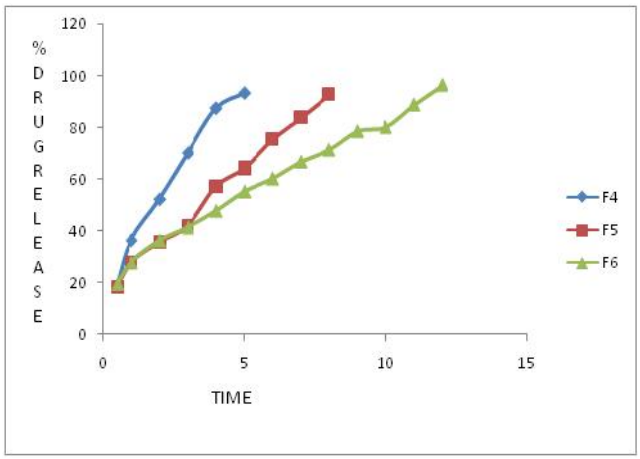

Figure 3: Dissolution profile of Hydrochlorthiazide HCl floating tablets (F4, F5, F6 formulations**).**

Table 5: Dissolution Data of Hydrochlorthiazide Tablets Prepared With HPMC K100M In Different Concentrations

Time **(hr)**	**Cumulative percent drug dissolved (n=3±sd)**		
	F7	**F8**	**F9**
0.5	18.81	19.89	14.21
1	29.02	28.04	18.87
2	35.70	35.43	27.19
3	43.32	41.65	35.66
4	49.25	47.18	43.32
5	55.28	53.81	51.06
6	60.92	58.89	57.13
7	66.08	64.53	63.63
8	70.44	69.43	69.71
9	77.22	72.83	73.34
10	80.90	79.98	79.27
11	87.83	83.52	82.86
12	91.90	88.65	85.97

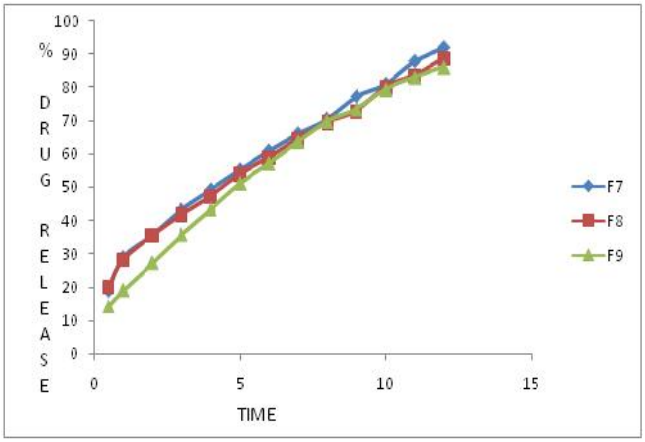

Figure 4: Dissolution profile of Hydrochlorthiazide HCl floating tablets (F7, F8, F9 formulations)

From the dissolution data it was evident that the formulations prepared with Guar gum as polymer were unable to retard the drug release up to desired time period i.e., 12 hours. Whereas the formulations prepared with HPMC K15M retarded the drug release in the concentration of 120 mg (F6) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 96.33 % in 12 hours with good floating lag time and floating buoyancy time. The formulations prepared with HPMC K 100M showed more retardation even after 12 hours they were not shown total drug release. Hence they were not considered.

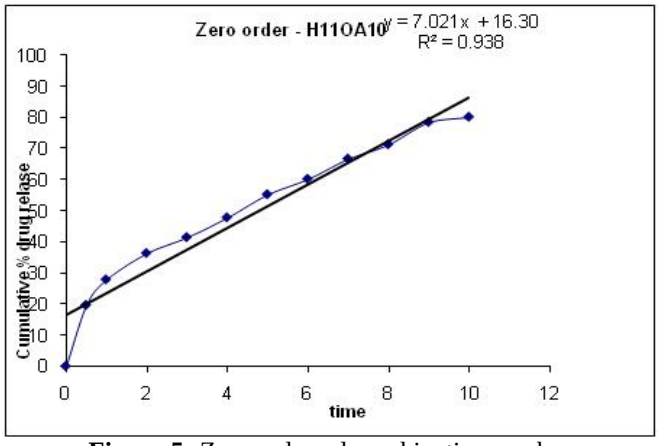

Figure 5: Zero order release kinetics graph

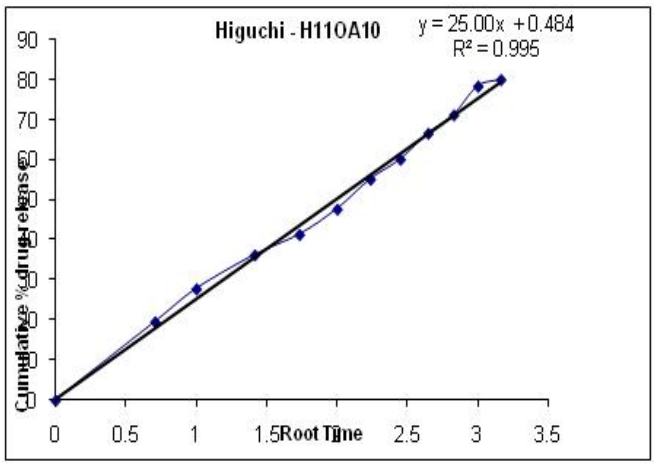

Figure 6: Higuchi release kinetics graph

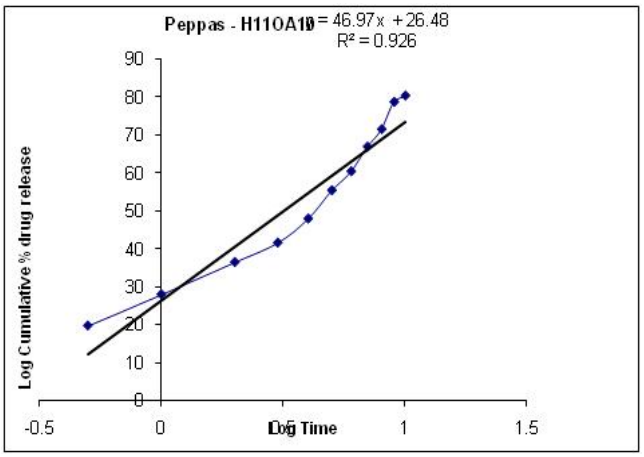

Figure 7: Kars mayer peppas graph

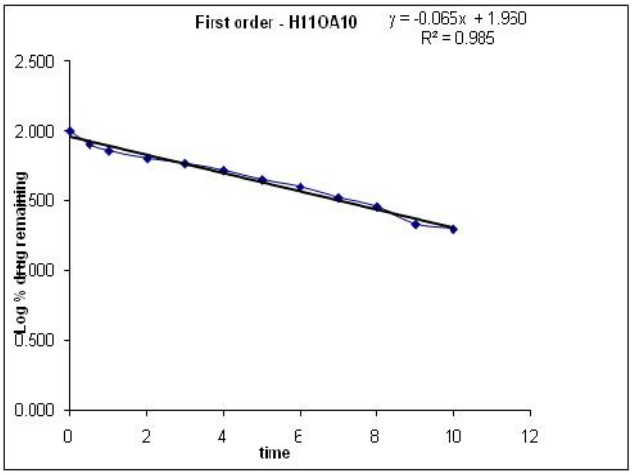

Figure 8: First order release kinetics graph

From the above graphs it was evident that the formulation F6 was followed Higuchi mechanism.

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 6: Formulation composition for floating tablets

Formulation No.	Hydrochlorthiazide	Guar gum	HPMC K15M	HPMC K100M	$NaHCO_3$	Mag. Stearate	Talc	MCC pH 102
F1	12.5	20	-----	-----	20	3	3	QS
F2	12.5	40	-----	-----	20	3	3	QS
F3	12.5	60	-----	-----	20	3	3	QS
F4	12.5	-----	20	-----	20	3	3	QS
F5	12.5	-----	40	-----	20	3	3	QS
F6	12.5	-----	60	-----	20	3	3	QS
F7	12.5	-----	-----	20	20	3	3	QS
F8	12.5	-----	-----	40	20	3	3	QS
F9	12.5	-----	-----	60	20	3	3	QS

All the quantities were in mg, total weight is 200 mg.

Pre-formulation 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	26.01	0.49±0.07	0.57±0.01	16.21±0.06	0.86±0.06
F2	24.8	0.56±0.06	0.62±0.05	16.87±0.05	0.98±0.05
F3	22.74	0.52±0.03	0.68±0.07	17.11±0.01	0.64±0.03
F4	25.33	0.54±0.04	0.64±0.08	17.67±0.08	1.12±0.04
F5	26.24	0.53±0.06	0.67±0.03	16.92±0.04	1.2±0.08
F6	26.12	0.56±0.05	0.66±0.06	17.65±0.09	1.06±0.09
F7	27.08	0.58±0.06	0.69±0.04	16.43±0.05	0.76±0.03
F8	25.12	0.48±0.05	0.57±0.02	17.97±0.02	1.15±0.09
F9	25.45	0.54±0.08	0.62±0.03	17.54±0.09	1.17±0.02

Table 8

Formulation codes	Weight variation (mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Flaoting lag time (min)
F1	212.5	4.5	0.52	3.8	99.76	4.0
F2	205.4	4.2	0.54	3.9	99.45	4.2
F3	198.6	4.4	0.51	3.9	99.34	4.5
F4	210.6	4.5	0.55	3.9	99.87	4.1
F5	209.4	4.4	0.56	3.7	99.14	4.0
F6	210.7	4.2	0.45	3.5	98.56	4.4
F7	202.3	4.1	0.51	3.4	98.42	4.5
F8	201.2	4.3	0.49	3.7	99.65	4.6
F9	298.3	4.5	0.55	3.6	99.12	4.7

Table 9: Release kinetics data for optimised formulation

Cumulative (%) Release Q	Time (T)	Log (%) Release	Log (T)	Log (%) Remain	Release Rate (Cumulative % Release / t)	1/CUM% Release	Papas log Q/100	% Drug Remaining
0	0			2.000				100
19.62	0.5	1.293	-0.301	1.905	39.240	0.0510	-0.707	80.38
27.86	1	1.445	0.000	1.858	27.860	0.0359	-0.555	72.14
36.35	2	1.561	0.301	1.804	18.175	0.0275	-0.439	63.65
41.45	3	1.618	0.477	1.768	13.817	0.0241	-0.382	58.55
47.8	4	1.679	0.602	1.718	11.950	0.0209	-0.321	52.2
55.25	5	1.742	0.699	1.651	11.050	0.0181	-0.258	44.75
60.24	6	1.780	0.778	1.599	10.040	0.0166	-0.220	39.76
66.73	7	1.824	0.845	1.522	9.533	0.0150	-0.176	33.27
71.34	8	1.853	0.903	1.457	8.918	0.0140	-0.147	28.66
78.52	9	1.895	0.954	1.332	8.724	0.0127	-0.105	21.48
80.17	10	1.904	1.000	1.297	8.017	0.0125	-0.096	19.83
88.75	11	1.948	1.041	1.051	8.068	0.0113	-0.052	11.25
96.33	12	1.984	1.079	0.565	8.028	0.0104	-0.016	3.67

4. Conclusion

In the present research work gastro retentive floating matrix formulation of Hydrochlorthiazide by using various hydrophilic polymers. Initially analytical method development was done for the drug molecule. Absorption maxima was determined based on that calibration curve was developed by using different concentrations. Gas generating agent sodium

bicarbonate concentration was optimized. Then the formulation was developed by using different concentrations of polymers of various grades of HPMC and Guar gum. The formulation blend was subjected to various pre-formulation 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 the formulations prepared by using Guar gum were unable to produce desired drug release, they were unable to retard drug release up to 12 hours. The formulations prepared with HPMC K 15 M retarded the drug release up to 12 hours in the concentration of 60 mg (F6).The formulations prepared with HPMC K100M were also retarded the drug release for more than 12 hours. Hence they were not considered. The optimized formulation dissolution data was subjected to release kinetics, from the release kinetics data it was evident that the formulation followed Higuchi mechanism of drug release.

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