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Design, Prepare, and *in vitro* Evaluation of Hydrochlorothiazide Floating Tablets

M Vijaya Laxmi [1*], Lingoju Manasa [2]
[1, 2] Associate Professor, Teegala Krishna Reddy College of Pharmacy, Medbowli, Meerpet, Saroornagar, Hyderabad, Telangana, India

* Corresponding Author: **M Vijaya Laxmi**

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Abstract
The main purpose of the study was to develop Hydrochlorothiazide floating tablets via non-effervescent technique using various polymers by direct compression. Before compression, the particulate powdered mixture was evaluated for pre-compression parameters. Compatibility among the formulation components was assessed by FTIR studies. FTIR studies revealed no interaction between the drug and polymers used. The prepared Hydrochlorothiazide tablets were evaluated for post-compression parameters, swelling index, floating lag time, *in vitro* buoyancy studies, and *in vitro* drug release studies. Optimized formulation (F4) revealed that tablet was constantly floating in the stomach region of the rabbit, thereby indicating improved gastric retention time for more than 8 hr. Consequently, all the findings and outcomes have showed that developed Hydrochlorothiazide floating tablets could be effectively used for floating drug delivery system.

Keywords: Hydrochlorothiazide, Polymers, Sodium Bi Carbonate and Citric Acid, FTIR Studies, Direct Compression Technique, *In vitro* Drug Release Studies

Introduction
Oral drug delivery is the most preferred route of drug delivery of pharmaceuticals encompassing number of diseases which have been successfully treated. Owing to its potential advantages including well-established delivery system, patient friendly, convenient, cost effective, and non-invasiveness, it has been the most favoured drug delivery system in pharmaceutical field [1]. Floating drug delivery systems have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased gastric retention time and control of the fluctuation in plasma drug concentration [2] Gastro retentive dosage form can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility of drugs that are less soluble in a high pH environment. Gastro retention helps to provide better availability of new products with suitable therapeutic activity and substantial benefits for patient [3]. Hydrochlorothiazide (HCT) is a thiazide diuretic and is adopted in the supervision of slight to modest hypertension. It remains precise marginally soluble in water holding a plasma half-life of 6h–14h and protein binding 67.9%. It remains variably absorbed from the gastrointestinal tract, eliminated rapidly by the kidney and primarily excreted in unchanged form in urine [4].

Materials
Hydrochlorothiazide was obtained from Hetero Lab, HYD. Ethyl cellulose and Eudragit RS 100 were procured from Synpharma Research Labs, Hyderabad, and other chemicals, and the reagents used were of analytical grade.

Methodology

FT-IR study [5]

Compatibility of the drug with excipients was determined by FT-IR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combined it with the excipients. The samples were taken for FT-IR study.

Formulation development

Table 1: Composition of Hydrochlorothiazide floating tablets

Ingredient	Formulations							
	F1	F2	F3	F4	F5	F6	F7	F8
Hydrochlorothiazide	10	10	10	10	10	10	10	10
Ethyl cellulose	10	20	30	40	-	-	-	-
Eudragit RS 100	-	-	-	-	10	20	30	40
Mannitol	60	50	40	30	60	50	40	30
Citric acid	5	5	5	5	5	5	5	5
Sodium bi carbonate	10	10	10	10	10	10	10	10
Magnesium stearate	3	3	3	3	3	3	3	3
Talc	2	2	2	2	2	2	2	2
Total weight	100	100	100	100	100	100	100	100

Preparation of Formulation [6]

Different tablet formulations were prepared by direct compression method. The formulations are composed of synthetic polymers. All powders were passed through 100-mesh sieve. The other excipients and the polymer were mixed uniformly. Drug was added to the polymers and other excipients for 20 min. The resulting mixture were mixed with magnesium Stearate and talc in polyethylene bag for 10 min. The lubricated granules were compressed using 8 mm punch (single punch tablet machine) in to tablets. Compression pressure was adjusted during tablet ting of each formula to get the tablet hardness in the range of 2.5 to 5 $Kg/cm^{2.}$ The total weight of tablet was kept at 100 mg.

Evaluation of tablets

- **Weight Variation test (U.S.P.):** Take 20 tablet and weighed individually. Calculate average weight and compare the individual tablet weight to the average. The tablet pass the U.S.P. test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit [7].
- **Hardness:** Tablet hardness and strength are the essential to see that the tablet can with the shock and stress during manufacturing packing and transportation, and while handled by the patient To test the hardness of the tablet Monsanto tester, Strong-cobb tester, the Pfizer tester, the Erweka tester, the Schleuniger tester are used [8].
- **Dimensionl Analysis:** The thickness and diameter of tablets was determined using vernier caliper. Twenty tablets from each batch were used and average values were calculated. Size and Shape It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by micrometer or by other device. Tablet thickness should be controlled within a ± 5% variation of standard value [9].
- **Floating lag time and total floating time:** Floating lag time (FLT) and total floating time (TFT) of floating tablets were measured visually in dissolution apparatus type II containing100 mL 0.1 N HCl with a paddle rotated at50 rpm (pH 1.2) at 37 ± 0.5 °C [10].
- **Dissolution Study:** *In vitro* drug release of the formulation was carried out using USP dissolution apparatus type II paddle type under sink condition with rotating speed of 50 rpm and at temperature of37 ± 0.5 °C. The dissolution medium used was 900ml 0.1NHCl. The samples were withdrawn at predetermined time intervals for period of 6hours and replaced with the fresh medium, suitably diluted and were analysed using UV/Visible spectrophotometer [11].

Disintegration Test (U.S.P.)

The U.S.P. device to test disintegration uses 6 glass tubes that are 3" long; open at the top and 10 mesh screens at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37 ± 2 0 C such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet. According to the test the tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass [12].

Drug release kinetics [13]

In order to describe the Drug release kinetics from individual tablet formulations, the corresponding dissolution data were fitted in various kinetic dissolution models:

Zero order, first order, and Higuchi respectively.

$Qt = Q0 + K0\ t$……..

Where, Qt is the amount of drug released at time t; Q0 the amount of drug in the solution at t = 0, (usually, Q0 = 0) and K0 the zero order release constant.

$\log Qt = \log Q\alpha + (K1 / 2.303)\ t$……..

Qα being the total amount of drug in the matrix and K1 the first order kinetic constant.

$Qt = KH.\ t\ ½$…….

Where,
KH is the Higuchi rate constant.
Further, to better characterise the mechanism of drug release from matrices, dissolution data were analyzed using the equation proposed by Korsmeyer and Peppas.

$Q\ (t-l)\ /Q\alpha = KK\ (t-l)n$…….

where, Qt corresponds to the amount of drug released in time t, *l* is the lag time (*l* = 2 hours), Qα is the total amount of drug that must be released at infinite time, KK a constant comprising the structural and geometric characteristics of the tablet, and n is the release exponent indicating the type of drug release mechanism.

Stability studies [14]

The success of an effective formulation can be evaluated only

through stability studies. The purpose of stability testing is to obtain a stable product which assures its safety and efficacy up to the end of shelf life at defined storage conditions and peak profile. The prepared Hydrochlorothiazide floating tablets were placed on plastic tubes containing desiccant and stored at ambient conditions, such as at room temperature, 40±2°c and refrigerator 2-8°c for a period of 90 days.

Results and Discussion

FT-IR Spectrum of Hydrochlorothiazide

FT-IR Spectra of Hydrochlorothiazide and F4 formulation were recorded. All these peaks have appeared in formulation and physical mixture, indicating no chemical interaction between Hydrochlorothiazide and polymer. It also confirmed that the stability of drug during microencapsulation process.

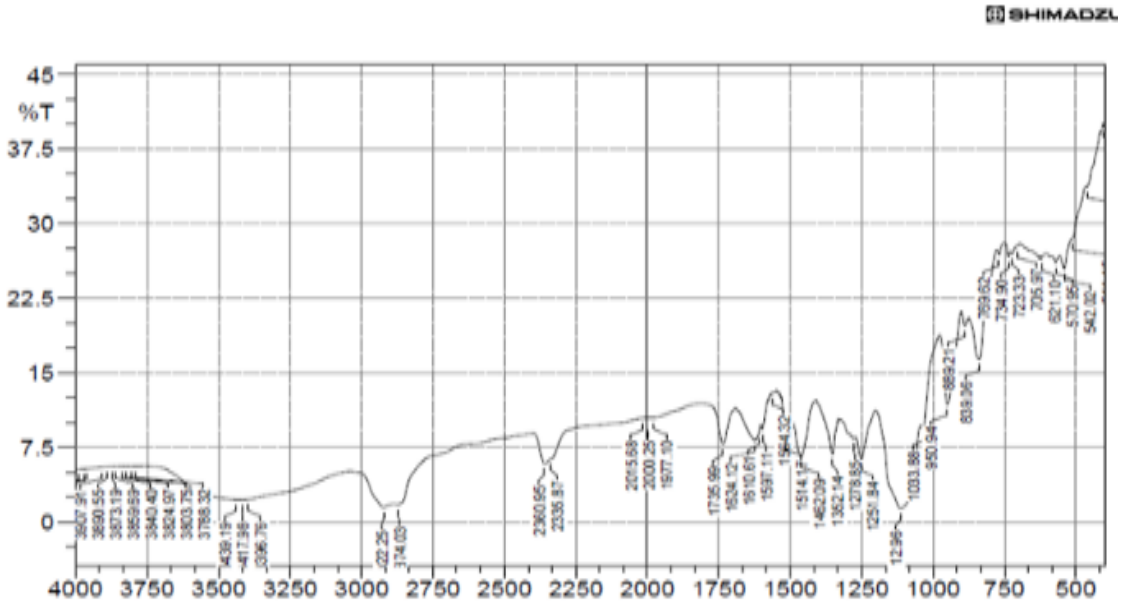

Fig 1: FT-IR Sample for Hydrochlorothiazide

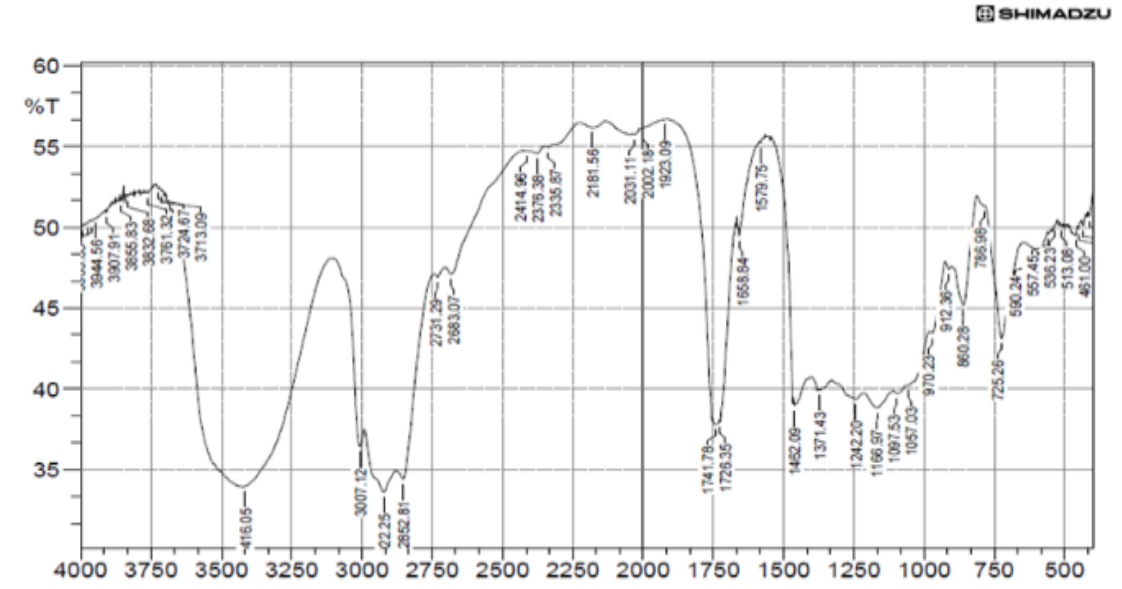

Fig 2: FT-IR Sample for physical mixture of drug and excipients

The IR spectrum of drug and Drug Excipients mixture was shown in respectively. In the present study, it has been observed that there is no chemical interaction between drug and the polymers used. From the figures it was observed that there were no changes in these main peaks in IR spectra of mixture of drug and polymers, which show there were no physical interactions because of some bond formation between drug and polymers. This further confirms the integrity of pure drug and compatibility of them with excipients.

Evaluation of the Prepared Tablets for Physical Parameters

All formulations were tested for Physical parameters like Hardness, thickness, Weight Variation, Friability and found to be within the Pharmacopoeial limits. The results of the tests were tabulated. The drug content of all the formulations was determined and was found to be within the permissible limit. This study indicated that all the prepared formulations were good.

Table 2: Evaluation parameters of Hydrochlorothiazide floating tablets

F.no	Weight variation	Thickness (mm)	Hardness (kg/cm^2	Friability	Content uniformity	Floating lag time (Sec)
F1	100±1.15	2.68±0.86	3.58±1.38	0.25±0.42	80.12±1.58	45±3.25
F2	99±1.57	2.92±0.28	3.46±1.40	0.42±0.53	79.63±1.37	50±3.32
F3	101±2.13	2.75±0.16	3.19±1.58	0.29±0.29	81.24±1.54	49±2.98
F4	100±2.89	2.63±2.15	3.28±1.17	0.35±0.32	86.92±1.32	43±2.69
F5	100±2.49	2.58±0.29	3.42±1.05	0.37±0.32	82.35±1.49	52±2.57
F6	99±2.47	2.49±0.24	3.17±1.42	0.26±0.32	79.63±1.53	47±2.65
F7	100±1.59	2.38±0.28	2.98±1.23	0.28±0.32	81.25±1.58	51±2.98
F8	101±2.16	2.27±0.31	3.20±1.03	0.32±0.32	83.55±1.62	48±3.47

Floating lag time

The floating tablets of Hydrochlorothiazide were prepared by using direct compression technique. Eight different formulations were prepared using different ratios of polymers. The prepared formulations were evaluated for floating lag time and buoyancy time. Sodium bicarbonate induced carbon dioxide generation in presence of dissolution medium (0.1 N HCl). It was observed that the gas generated is trapped and protected within the matrix, formed by polymers, thus density of the tablet decreased and it becomes buoyant. The floating lag time of the optimized formulation F4 was 43±2.69 sec.

Fig 3: Floating lag time

***In vitro* Dissolution studies**

The samples were withdrawn at predetermined time points, and were analyzed spectrophotometrically at 250 nm

Table 3: *In vitro* drug release of Hydrochlorothiazide floating tablets

Time	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	12.42±1.28	13.25±2.28	13.70±1.27	15.65±2.69	14.42±1.50	18.40±2.20	14.85±1.69	14.89±1.17
2	25.90±2.10	23.14±2.16	24.70±2.68	28.68±2.64	25.18±2.24	29.92±1.38	23.48±2.20	22.71±1.23
3	32.15±2.51	29.60±2.95	30.25±2.43	30.88±2.67	30.22±1.26	33.58±1.19	32.27±1.18	34.18±1.27
4	40.19±1.15	35.62±2.25	44.58±1.98	42.85±1.47	43.28±1.58	45.26±2.69	43.61±2.68	45.85±1.26
5	52.16±2.23	49.21±2.17	58.93±1.24	57.18±1.28	50.42±2.35	59.63±1.17	57.27±2.15	59.27±2.30
6	63.95±1.85	70.14±1.83	65.39±2.30	64.56±1.54	62.10±1.10	68.15±2.58	64.46±2.03	66.72±1.98
7	70.18±2.29	73.01±1.84	70.25±2.21	72.17±2.10	73.53±2.51	78.98±1.58	79.68±1.25	73.43±1.57
8	85.95±2.13	89.20±2.59	89.69±1.57	94.91±1.19	91.75±1.58	93.26±1.85	90.25±1.24	86.92±2.20

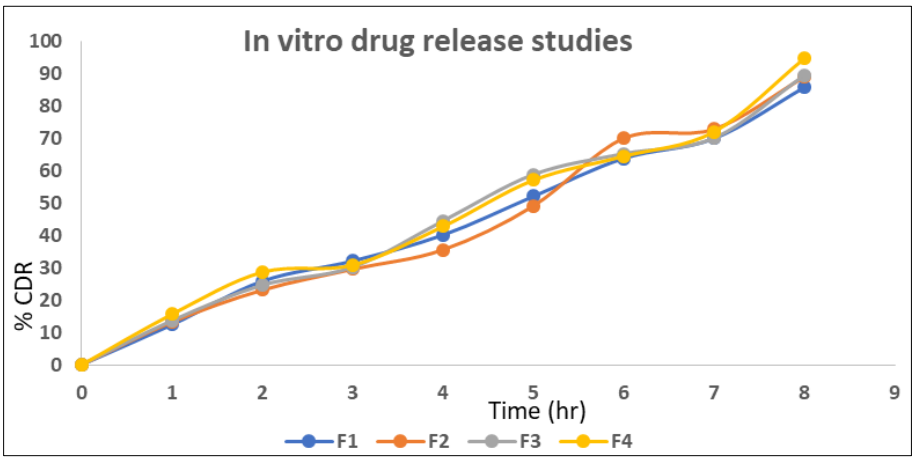

Fig 4: *In vitro* drug release for (F1-F4) formulations

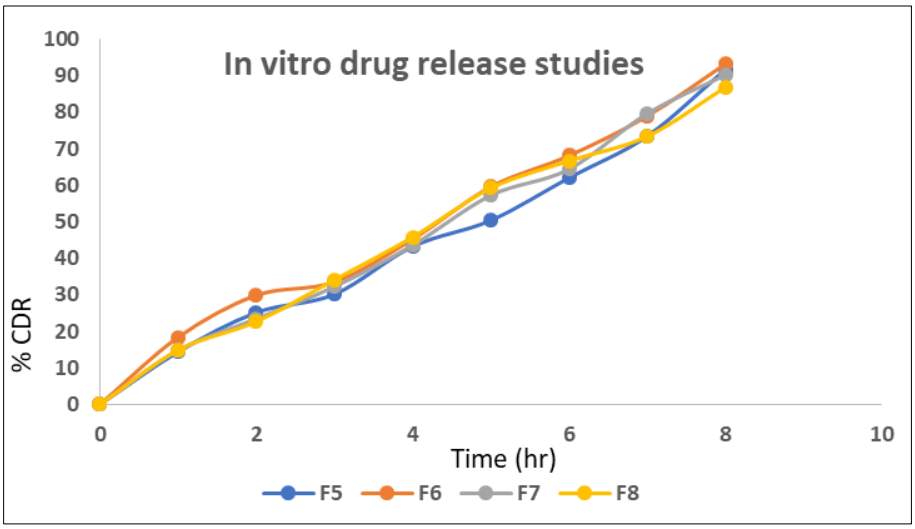

Fig 5: *In vitro* drug release for (F5-F8) formulations

Drug release kinetics

The kinetic of drug release for formulation F6 was calculated and plotted. The formulation F6 follows first order release kinetics and the drug release mechanism was found to be non-Fickan anomalous diffusion.

***In-vitro* Dissolution Study and Kinetic modelling of drug release**

The results obtaining *in vitro* release studies were plotted in different model

1. Zero order rate kinetics
2. First Order rate Kinetics
3. Higuchi's models
4. Krosmayer peppas

Zero order kinetics

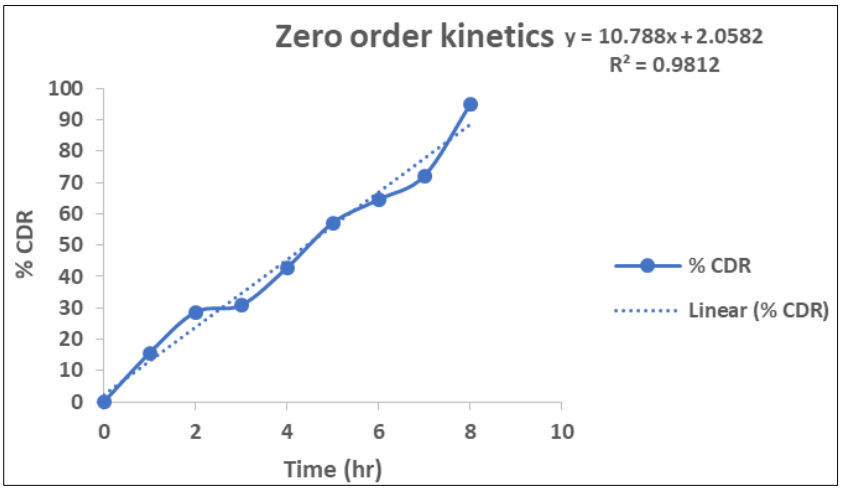

Fig 6: Zero order kinetics of optimized formulation

First order kinetics

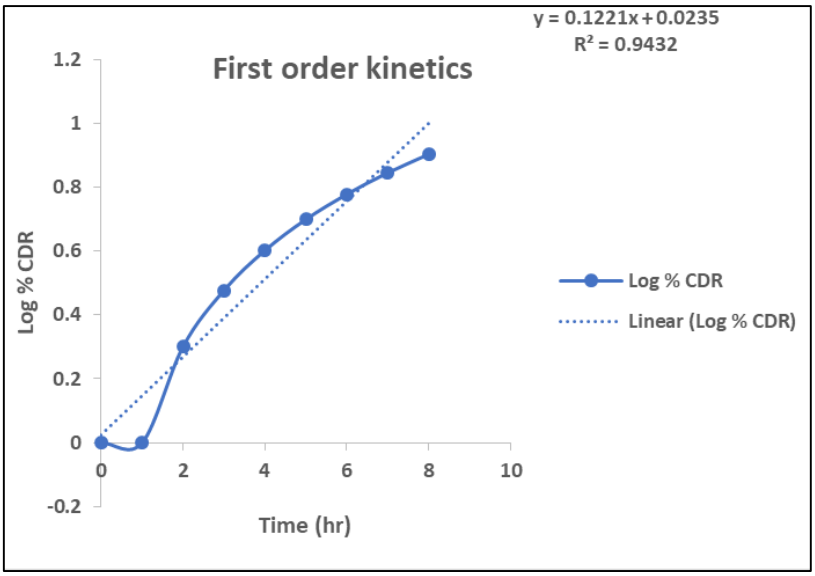

Fig 7: First order kinetics of optimized formulation

Higuchi model

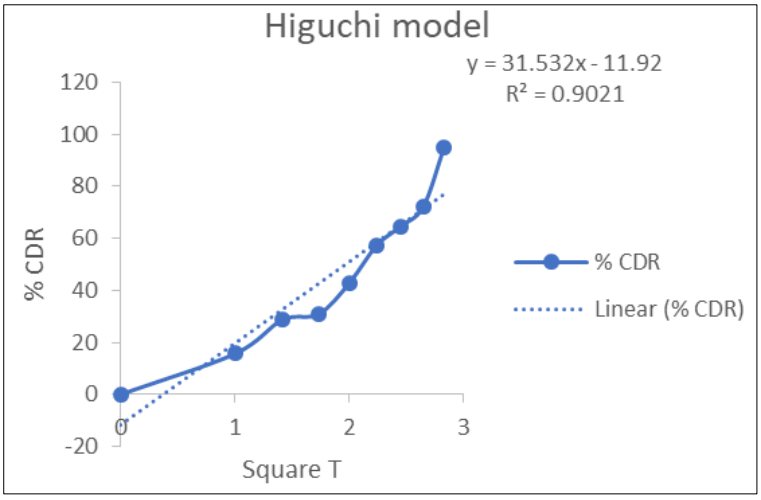

Fig 8: Higuchi model of optimized formulation

Krossmayer peppas

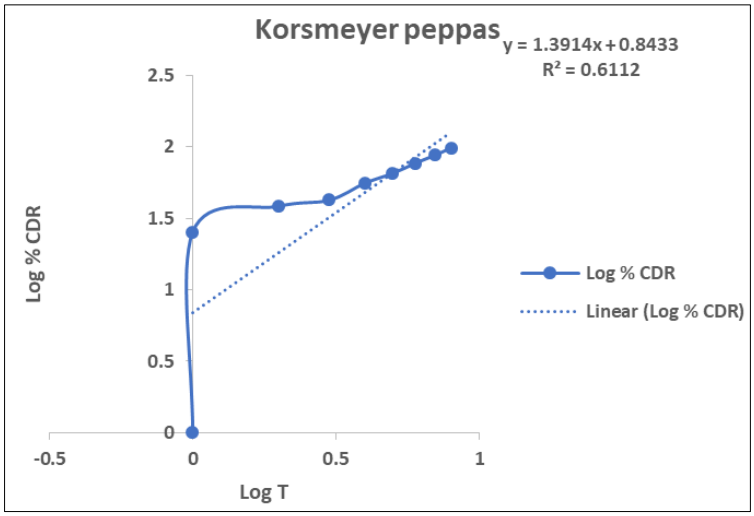

Fig 9: Krossmayer peppas of optimized formulation

The values of *in vitro* release were attempted to fit into various mathematical models. Plots of zero order, first order, Higuchi matrix, Peppas were respectively

Stability Study

There was no significant change in physical and chemical properties of the tablets of formulation F-4 after 90 days. Parameters quantified at various time intervals were shown.

Optimized formulations F4 was selected for accelerated stability studies as per ICH guidelines. The floating tablets were observed for % cumulative drug release of the formulation was found to be decreasing.

Table 4: Stability study for optimized formulation

S.NO	Time in days	Physical changes	Mean % drug release		
			Mouth dissolving tablet		
			25^0C/60%	30^0C/75%	40^0C/75%
1.	01	No Change	94.91±1.19	94.91±1.19	94.91±1.19
2.	30	No Change	93.58±1.25	93.56±1.47	93.65±1.68
3.	60	No Change	92.59±1.08	92.72±1.29	92.68±2.23
4.	90	No Change	91.50±1.31	91.25±1.35	91.72±1.30

Conclusion

The objective of the present study is to develop a Floating tablets of Hydrochlorothiazide. In this present study an attempt was made to increase the GI residence time of Hydrochlorothiazide, as the drug is having less gastric residence time, by formulating in to Floating tablets. Systematic studies were conducted using different concentration of rate releasing different polymers for extending the drug release in upper GIT. All the prepared systems were evaluated for the different properties. Before the preparation of tablets, preformulation studies to find out the micromeritic properties to assess flowability, compressibility properties and solubility studies and all the formulations gave good results for above preformulation studies. Formulated tablets gave satisfactory results for various physical tablet evaluation parameters like tablet dimensions, hardness, friability, weight variation, buoyancy, content uniformity, all the formulations were found within the permissible range. Among all the formulations (F1-F8), it was observed that formulation-4 has shown better buoyancy and dissolution profile. So Formulation-4 was found to be the best formulation among others.

References

1. Kwon GS, Okano T. Polymeric micelles as new drug carriers. Adv Drug Deliv Rev. 1996;21(2):107–116.
2. Shah SH, Patel JK, Patel NV. Stomach specific floating drug delivery system: a review. Int J Pharm Tech Res. 2009;1:623–633.
3. Ahsan. Formulation optimization and *in-vitro* evaluation of oral floating captopril matrix tablets using factorial design. Trop J Pharm Res. 2015 Oct;14(10):1737.
4. Mujahid M, Baboota S, Ali J. Development and validation of stability indicating HPTLC method for the simultaneous determination of hydrochlorothiazide and losartan in fixed dose combination. Nov Sci Int J Pharm Sci. 2012.
5. Ramu. Formulation and evaluation of gastroretentive floating bioadhesive tablets of hydrochlorothiazide. Asian J Pharm Clin Res. 2017;10(5).
6. Raza A, Hayat U, Wang HJ, Wang JY. Preparation and evaluation of captopril loaded gastro-retentive zein based porous floating tablets. Int J Pharm. 2020;579:119176.
7. Prajapati PH, Nakum VV, Patel CN. Formulation and evaluation of floating matrix tablet of stavudine. Int J Pharm Investig. 2012;2(2):83–89.
8. Afzal GM. Formulation and evaluation of floating fenoverine tablets. Bull Environ Pharmacol Life Sci. 2023;12(7):164–174.
9. Pahwa. Formulation and *in-vitro* evaluation of effervescent floating tablets of an antiulcer agent. J Chem Pharm Res. 2012;4(2):1066–1073.
10. Kavitha K. Formulation and evaluation of ranitidine floating tablets. Int J Pharm Chem Biol Sci. 2013;3(3):761–766.
11. Bravo-Osuna I, Vauthier C, Farabollini A, Palmieri GF, Ponchel G. Mucoadhesion mechanism of chitosan and thiolated chitosan-poly(isobutyl cyanoacrylate) core-shell nanoparticles. Biomaterials. 2007;28:2233–2243.
12. Bulgarelli E, Forni F, Bernabei MT. Effect of matrix composition and process conditions on casein-gelatin beads floating properties. Int J Pharm. 2000;198:157–165.
13. Burton S, Washington N, Steele RJ, Musson R, Feely L. Intragastric distribution of ion-exchange resins: a drug delivery system for the topical treatment of the gastric mucosa. J Pharm Pharmacol. 1995;47:901–906.
14. Kumar MS, *et al*. Formulation and *in vitro* evaluation of gastro retentive floating tablets of glipizide. Int J Innov Pharm Res. 2011;2(3):151–155.