



## **Design and characterisation of sustain release gastro retentive floating tablets of Diltiazem Hydrochloride**

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### **Abstract**

Gastroretentive drug delivery systems are the systems which are retained in the stomach for a longer period of time and thereby improve the bioavailability of drugs. Diltiazem Hydrochloride, is a Calcium channel blocker, an anti-hypertension and anti-anginal drug, Diltiazem Hydrochloride undergoes an extensive biotransformation, mainly through cytochrome P-450 CYP3A, which results in less than 4% of its oral dose being excreted unchanged in urine. Suffers from poor bioavailability (~30% to 40%) owing to an important first pass metabolism. It has an elimination half-life of 3.5 hrs and an absorption zone from the upper intestinal tract. Thus the present work is aimed to formulate floating tablets of Diltiazem Hydrochloride using an effervescent approach for gastroretentive drug delivery system. Floating tablets were prepared using direct compression technique using Hydrophilic polymer like HPMC K4M, HPMC K15M and hydrophobic polymer like Ethylcellulose as matrix materials in various quantities (%w/w), sodium bicarbonate, citric acid, magnesium stearate, talc and lactose in varying ratio to formulate the floating tablets. Observations of all formulations for physical characterization had shown that, all of them comply with the specification of official pharmacopoeias and/or standard reference. It was observed that tablets of batch F6 followed the results obtained, it was concluded that the formulation F6 is the best formulations as the extent of drug release was found to be around 99.81 % at the desired time 12 hrs.

**Key words-** Floating tablets, swelling index, Diltiazem Hydrochloride, in-vitro buoyancy studies

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### **Introduction**

The oral drug delivery is by far the most preferable route of drug delivery system, due to ease of administration, patient compliance, and flexibility in formulation etc. From immediate release to

site specific delivery, oral dosage form have really progressed. It is evident from the recent scientific and patient literature that an increased interest in novel dosage forms that are retained in the stomach for a prolonged period of time exists today in academic and industrial research groups. One of the most feasible approaches for achieving a prolonged and predictable drug delivery in the GI tract is to control the gastric residence time (GRT), i.e. gastro retentive dosage form (GRDS or GRDF). Effective oral drug delivery may depend upon the factors such as gastric emptying process, gastro intestinal transit time of dosage form, drug release from the dosage form and site of absorption of drug. Most of the oral dosage forms possess several physiological limitations such as variable gastrointestinal transit, because of variable gastric emptying leading to non-uniform absorption profiles, incomplete drug release and shorter residence time of the dosage form in the stomach. The gastric emptying of dosage forms in humans is affected by several factors because of which wide inter- and intra-subject variations are observed. Since many drugs are well absorbed in the upper part of the gastrointestinal tract, such high variability may lead to non-uniform absorption and makes the bioavailability unpredictable. Among the various gastro retentive systems, gastric floating drug delivery systems (GFDDS) offer numerous advantages over the gastric retentive systems. These systems have a density lower than the gastric fluids and thus 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 a desired rate from the stomach. Cardiovascular diseases are one of the life threatening diseases of the world. Angina pectoris, hypertension and cardiac failure are the commonest diseases and require constant monitoring. Calcium channel blockers are emerging as a very important group in the management of angina pectoris and hypertension. Diltiazem hydrochloride is a calcium channel blocker belonging to the benzothiazepine family. It is widely prescribed for the treatment of hypertension and angina. Diltiazem Hydrochloride undergoes an extensive biotransformation mainly through cytochrome P-450 CYP3A, which results in less than 4% of its oral dose being excreted unchanged in urine. Bioavailability of Diltiazem Hydrochloride is ~30% to 40% owing to an important first pass metabolism. It has an elimination half-life of 3-4.5 hours and has an absorption zone from the upper intestinal tract. Efficacy of the administered dose may get reduced due to incomplete drug release from the device above the absorption zone. The dosage is 30mg, 4 times a day and increased as necessary up to 360mg/day in divided doses. Diltiazem Hydrochloride requires multiple daily drug dosages in order to maintain adequate plasma concentrations. Due to short half-life of Diltiazem Hydrochloride, frequent administration is required. These two drawbacks can be overcome by developing a floating dosage form to be remained buoyant in the stomach. Therefore, it is a suitable model candidate for gastroretentive formulation. The gastroretentive drug delivery systems can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the gastrointestinal tract. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bio-availability.

## **Methods and Materials**

Diltiazem Hydrochloride was obtained as a generous gift by Central Drug Research Laboratory, Lucknow (U.P., India) respectively and HPMC K4M, HPMC K15M was gifted by Colorcon, Mumbai, ethyl cellulose, Sodium bicarbonate was gifted by Nice chemicals laboratory, Citric

acid (anhydrous), Magnesium stearate was gifted by Central Drug House (P) Ltd. India, Talc, Spray dried lactose procured by Vardhman Healthcare, Mullana, India.

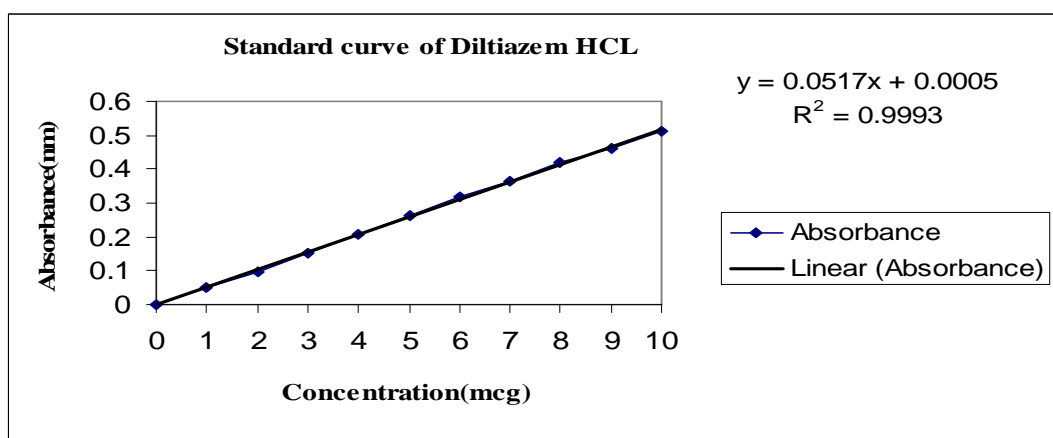
***Preparation of standard curve of diltiazem hydrochloride:***

100 mg of Diltiazem Hydrochloride was accurately weighed and transferred to a 100ml volumetric flask containing 100 ml of 0.1 N HCl solution and shaken to dissolve. The solution resulted is  $\approx 1000 \mu\text{g/ml}$ . Then 10 ml of this solution is transferred to another volumetric flask to obtain solution of  $100 \mu\text{g/ml}$  served as stock. Then again 10 ml of this solution is transferred to another volumetric flask to obtain solution of  $10 \mu\text{g/ml}$  and the absorbance was taken on double beam U.V. spectrophotometer using  $\lambda_{\text{max}}$  at 236.80nm. The absorbance values were plotted against concentration ( $\mu\text{g/ml}$ ) to obtain the standard calibration curve.

***Preparation of 0.1 N HCl:*** Dilute 8.5 ml of concentrated HCl in 1000 ml of distilled water to get 0.1 N HCl.

***Standard calibration curve of diltiazem hydrochloride:***

Standard calibration curve of Diltiazem Hydrochloride was determined by plotting absorbance V/s concentration at 236.80 nm. And it follows the Beer's law.



**Figure 1. Standard curve of Diltiazem Hydrochloride in 0.1N HCL solution(pH 1.2) at  $\lambda_{\text{max}}$  236.80nm**

***Formulation of floating tablets:***

Diltiazem Hydrochloride was used with various grades of HPMC & Ethylcellulose in varying concentration to formulate the floating tablets. Lactose was used as a diluents in the preparation of the tablets. Sodium bicarbonate was incorporated into the tablets to aid buoyancy of the tablets due to liberation of  $\text{CO}_2$  when tablets come in contact with acidified dissolution medium. Citric acid was incorporated in the formulation to nullify the effect of the acidic dissolution media on the drug release. The level of the drug in all of the formulation was kept constant at 30% and tablet weight was adjusted so as to contain 90 mg of Diltiazem Hydrochloride in each tablet.

Different tablets formulations were prepared by direct compression technique. All the powders were passed through #80 mesh sieve. Required quantity of drug and low-density polymer and

hydrophobic polymer ethylcellulose were mixed thoroughly. Talc (2% w/w) and magnesium stearate (2% w/w) were finally added as glident and lubricant respectively. The blend was directly compressed (9mm diameter punches) using tablet compression machine. The tablet weight was adjusted to 300 mg and 25 tablets for each batch were prepared. The formula for the different batches is given in the table no 8.

**Table 1. Formula for formulation F1 –F12**

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
<b>Diltiazem Hydrochloride</b>	90	90	90	90	90	90	90	90	90	90	90	90
<b>HPMC K4M</b>	75	--	37.7	60	--	30	45	--	22.5	90	--	--
<b>HPMC K15M</b>	--	75	37.5	--	60	30	--	45	22.5	--	90	--
<b>Ethylcellulose</b>	15	15	15	30	30	30	45	45	45	--	--	90
<b>Sodium bicarbonate</b>	30	30	30	30	30	30	30	30	30	30	30	30
<b>Citric acid</b>	15	15	15	15	15	15	15	15	15	15	15	15
<b>Magnesium Stearate</b>	6	6	6	6	6	6	6	6	6	6	6	6
<b>Talc</b>	6	6	6	6	6	6	6	6	6	6	6	6
<b>Lactose</b>	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
<b>Total Weight</b>	300	300	300	300	300	300	300	300	300	300	300	300

- All quantities are in mg.
- All the batches contained 2% w/w talc and 2% w/w magnesium stearate.
- Each tablet contains uniform weight of 300 mg.

### ***Evaluation of floating tablets of diltiazem hydrochloride***

#### ***1) Pre-compression parameters:***

##### ***a) Determination of bulk density and tapped density***

Both bulk density (BD) and tapped density (TD) was determined. A quantity of 2 gm of powder blend from each formula, previously shaken to break any agglomerates formed, was introduced in to 10 ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted. BD and TD were calculated using the following equations.

$$\text{Bulk density} = W/V_o$$

$$\text{Tapped density} = W/V_f$$

Where, W = wt. of powder,  $V_o$  = initial volume, W = wt. of powder,  $V_f$  = final volume.

**b) Compressibility index**

The Compressibility index and Hausner ratio are measures of the propensity of a powder to be compressed. As such, they are measures of the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index and the Hausner Ratio. The compressibility index and Hausner ratio may be calculated using measured values for bulk density (Db) and tapped density (Dt) as follows:

$$\text{Compressibility index} = \frac{Dt - Db}{Dt} \times 100$$

$$\text{Hausner ratio} = \frac{Dt}{Db}$$

Where Db= Bulk density, Dt= Tapped density

**c) Angle of repose**

The angle of repose of powder blend was determined by the funnel method. The accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated.

The flow characteristics are measured by angle of repose. Improper flow of powder is due to frictional forces between the particles. These frictional forces are quantified by angle of repose.

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane.

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

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

Where h = height of pile, r = radius of the base of the pile,  $\theta$  = angle of repose

**2). post- compression parameters:****I. Tablet Hardness**

The crushing strength Kg/cm<sup>2</sup> of prepared tablets were determined for tablets of each batch by using Monsanto tablet hardness tester. Hardness indicates the ability of a tablet to withstand mechanical shocks while handling.

**II. Tablet Thickness**

The thickness of the tablets was determined by using vernier calipers. Five tablets were used, and average values were calculated.

**III. Friability Test.**

The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed ( $W_0$  initial) and transferred into friabilator. The

friabilator was operated at 25rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again ( $W_{\text{final}}$ ). The % friability was then calculated by

$$\%F = (1 - W/W_0) \times 100$$

Where,  $W_0$  = weight of tablet before test,  $W$  = weight of tablet after test.

#### IV. Weight variation test

To study weight variation twenty tablets of the formulation were weighed using a Sartorius electronic balance and the test was performed according to the official method. Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation.

**Table No.2. Percentage deviation allowed under weight variation**

Percentage deviation allowed under weight variation test.	
Average weight of tablet (X mg)	Percentage deviation
$X < 80$ mg	10
$80 < X < 250$ mg	7.5
$X > 250$ mg	5

#### V. Uniformity of Content

Five randomly selected tablets were weighed and powdered. The powder equivalent to average weight of tablets was weighed and drug was transferred in a 250ml flask containing 100ml of 0.1N HCl (pH 1.2). The flask was shaken on a flask shaker for 24 hours and was kept for 12 hours for the sedimentation of undissolved materials.

The solution were filtered through Whatman filter paper. 10ml of this filtrate was taken and appropriate dilution was made. The samples were analyzed at 236.80 nm using UV visible spectrophotometer. The drug content was determined from the standard curve prepared at  $\lambda_{\text{max}}$  236.8 nm.

#### VI. In Vitro Buoyancy Test

The prepared tablets were subjected to *in vitro* buoyancy test by placing them in 250 ml beaker containing 200ml 0.1 N HCl (pH 1.2, temp.  $37 \pm 0.5$  °C). The time between introduction of the dosage form and its buoyancy in the medium and the floating durations of tablets was calculated for the determination of lag time and total buoyancy time by visual observation. The Time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT) Table no.4

#### VII. Swelling index

Swelling of tablet excipients particles involves the absorption of a liquid resulting in an increase in weight and volume. Liquid uptake by the particle may be due to saturation of capillary spaces within the particles or hydration of macromolecule. The liquid enters the particle through pores and bind to large molecule; breaking the hydrogen bond and resulting in the swelling of particle. The extent of swelling can be measured in terms of weight gain by the tablet.

Each tablet from all formulations are pre-weighed and allowed to equilibrate with 0.1N HCL (pH-1.2) for 5hr, was then removed, blotted using tissue paper and weighed. The swelling index was then calculated using the formula:

$$\text{Swelling index } WU = \frac{(W_t - W_0)}{W_0} \times 100$$

$W_0$   
Where,  $W_t$  = Weight of tablet at time t,  $W_0$  = Initial weight of tablet

#### *VIII. Effect of hardness on Buoyancy Lag Time:-*

Formulation FT6 was selected to study the effect of hardness on buoyancy lag time. The tablets of batch 6 were compressed at different compression pressures to get the hardness of 5kg/cm<sup>2</sup>, 6kg/cm<sup>2</sup>, 7kg/cm<sup>2</sup>, 8kg/cm<sup>2</sup> and 9kg/cm<sup>2</sup>. The tablets were evaluated for Buoyancy Lag Time. The method followed is same as that of Buoyancy test.

#### *IX. In vitro Dissolution Study*

The dissolution study was carried out using USP II (paddle method) apparatus in 900 ml of 0.1 N HCl (pH 1.2) for 12 hours. The temperature of the dissolution medium was kept at 37± 0.5°C and the paddle was set at 100 rpm. 10 ml of sample solution was withdrawn at specified interval of time and filtered through Whatman filter paper. And the sample were replaced with fresh dissolution medium. The sample diluted to a suitable concentration with 0.1 N HCL. The absorbance of the withdrawn samples was measured at  $\lambda_{\text{max}}$  236.80 nm using a Shimadzu UV-1601 UV/VIS double beam spectrophotometer.

#### *Evaluation of tablet formulations:*

##### *I. Pre-compression Parameters:*

- a. *Angle of Repose ( $\theta$ ):-* The angle of repose for the formulated blend was carried out and the results were shown in table no.3. It concludes all the formulations blend was found to be in the range 21° to 25°.
- b. *Compressibility Index: -* Compressibility index was carried out, it found between 9.38% to 15.94% indicating the powder blend have the required flow property for compression.

##### *II. Post-compression Parameters:*

###### *a) Shape of the tablet:-*

Microscopic examinations of tablets from F1 to F12 were found to be circular shape with no cracks.

###### *b) Hardness test:-*

The measured hardness of tablets of each batch ranged between 4.8 to 5.6kg/cm<sup>2</sup>. This ensures good handling characteristics of all batches.

###### *c) Friability Test:-*

The values of friability test were tabulated in Table no.12. The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

***d) Weight Variation Test:-***

The percentage weight variations for all formulations were tabulated. All the formulated (F1 to F12) tablets passed weight variation test as the % weight variation was within the pharmacopoeial limits of  $\pm 5\%$  of the weight. The weights of all the tablets were found to be uniform with low standard deviation values.

***e) Drug Content Uniformity:-***

The percentage of drug content for F1 to F12 was found to be between 97.7% to 99.8% of Diltiazem Hydrochloride, it complies with official specifications.

***In vitro Buoyancy Study:-***

On immersion in 0.1N HCL solution pH (1.2) at 37<sup>0</sup>C, the tablets floated, and remained buoyant without disintegration. Table no.5 shows the results of Buoyancy study. From the results it can be concluded that the batch containing HPMC K4M or HPMC K15M polymer and Ethylcellulose showed good Buoyancy lag time (BLT) and Total floating time (TFT). Formulation F3, F6, F9 containing HPMC K4M, HPMC K15M and Ethylcellulose showed good BLT of 135,120,165 sec. respectively, while the formulation F12 containing Ethylcellulose (alone) did not float. This may be due to the nature of polymer and gas generating agent, which were kept constant in the present study. The gas generated cannot be entrapped inside the gelatinous layer, and it escapes leading to variation in BLT and TFT.

***Swelling Study:-***

Swelling study was performed on all the batches (F1 to F12) for 5 hr. From the results it was concluded that swelling increases as the time passes because the polymer gradually absorb water due to hydrophilicity of polymer. The outermost hydrophilic polymer hydrates and swells and a gel barrier are formed at the outer surface. As the gelatinous layer progressively dissolves and/or is dispersed, the hydration swelling release process is continuous towards new exposed surfaces, thus maintaining the integrity of the dosage form.

In the present study, the higher swelling index was found for tablets of batch F6 containing HPMC K4M, HPMC K15M and Ethylcellulose having nominal viscosity of more than 1, 04,000 cps. Thus, the viscosity of the polymer had major influence on swelling process, matrix integrity, as well as floating capability, hence from the above results it can be concluded that linear relationship exists between swelling process and viscosity of polymer.

***Effect of hardness on Buoyancy Lag Time:-***

The effect of hardness on buoyancy lag time for batch F6 was studied. The results of floating lag time of tablets with hardness of 4 kg/cm<sup>2</sup>, 5kg/cm<sup>2</sup>, 6kg/cm<sup>2</sup>, 7kg/cm<sup>2</sup> and 8 kg/cm<sup>2</sup> were 90,120,168,230 and 300 sec. respectively. Buoyancy of the tablet were influenced by both the swelling of the hydrocolloid particle on surface when it contacts the gastric fluid which in turn results in an increase in the bulk volume and porosity buoyancy lag time will increases when the hardness increases, at high compressed, reduces of porosity of tablets occurs, the compacted hydrocolloid particles on the surface of the tablet cannot hydrate rapidly when the tablet reaches the gastric fluid and as a result, the capability of the tablet to float is significantly reduced.

*Evaluation of granules:*

<b>Table no.3 → Pre-compression parameters of Formulation F<sub>1</sub> – F<sub>12</sub></b>					
<b>Powder blend Batch no.</b>	<b>Bulk density (g/ml)</b>	<b>Tapped density (g/ml)</b>	<b>Compressibility Index (%)</b>	<b>Hausner's Ratio</b>	<b>Angle of Repose (°)</b>
<b>F1</b>	0.454	0.501	9.38	1.10	21°
<b>F2</b>	0.452	0.519	12.90	1.15	22°
<b>F3</b>	0.449	0.503	10.74	1.12	21°
<b>F4</b>	0.451	0.526	14.25	1.16	24°
<b>F5</b>	0.450	0.530	15.10	1.18	24°
<b>F6</b>	0.448	0.533	15.94	1.18	25°
<b>F7</b>	0.453	0.523	13.38	1.15	23°
<b>F8</b>	0.452	0.518	12.74	1.14	24°
<b>F9</b>	0.452	0.537	15.82	1.18	22°
<b>F10</b>	0.455	0.522	12.83	1.14	22°
<b>F11</b>	0.451	0.527	14.42	1.16	21°
<b>F12</b>	0.452	0.535	15.32	1.18	23°

*Evaluation of tablets*

<b>Table no.4 → Post-compression parameters of Formulations F<sub>1</sub> – F<sub>12</sub></b>					
<b>Tablets Batch</b>	<b>Weight variation test</b>	<b>Friability (%)</b>	<b>Hardness (kg/cm<sup>2</sup>)</b>	<b>Thickness (mm)</b>	<b>Drug Content (%)</b>
<b>F1</b>	Pass	0.42	5.5	3.23	97.8
<b>F2</b>	Pass	0.43	5.6	3.10	98.3
<b>F3</b>	Pass	0.33	5.4	3.06	98.6
<b>F4</b>	Pass	0.23	5.0	3.13	98.0
<b>F5</b>	Pass	0.26	4.8	3.16	97.7
<b>F6</b>	Pass	0.39	5.0	3.10	99.8
<b>F7</b>	Pass	0.30	4.9	3.06	98.2
<b>F8</b>	Pass	0.36	4.93	3.23	98.1
<b>F9</b>	Pass	0.29	4.8	3.13	97.9
<b>F10</b>	Pass	0.32	5.0	3.16	98.0
<b>F11</b>	Pass	0.43	5.0	3.03	99.4
<b>F12</b>	pass	0.29	4.8	3.16	98.5

(n=3, the data represents the mean of three observations)

*In vitro buoyancy studies***Table no.5. In vitro Buoyancy study of formulations F1-F12**

Batch	Buoyancy Lag Time(sec.)	Total Floatation time(hrs.)
F1	100	12
F2	120	12
F3	150	12
F4	120	12
F5	125	>12
<b>F6</b>	132	>12
F7	140	>12
F8	155	>12
F9	170	>12
F10	150	11
F11	165	10
F12	---	---

**Table no.6. Swelling Index of Tablets of Batches F1 to F12**

Batch	TIME (HRS)					
	0	1	2	3	4	5
<b>F1</b>	0	42	55	60	70	88
<b>F2</b>	0	48	61	72	83	90
<b>F3</b>	0	35	48	55	70	79
<b>F4</b>	0	45	59	68	82	92
<b>F5</b>	0	32	43	57	63	78
<b>F6</b>	0	46	55	69	85	93
<b>F7</b>	0	36	48	59	67	89
<b>F8</b>	0	45	55	69	74	86
<b>F9</b>	0	33	45	58	71	88
<b>F10</b>	0	28	42	54	68	79
<b>F11</b>	0	38	48	60	76	86
<b>F12</b>	0	49	61	72	82	92

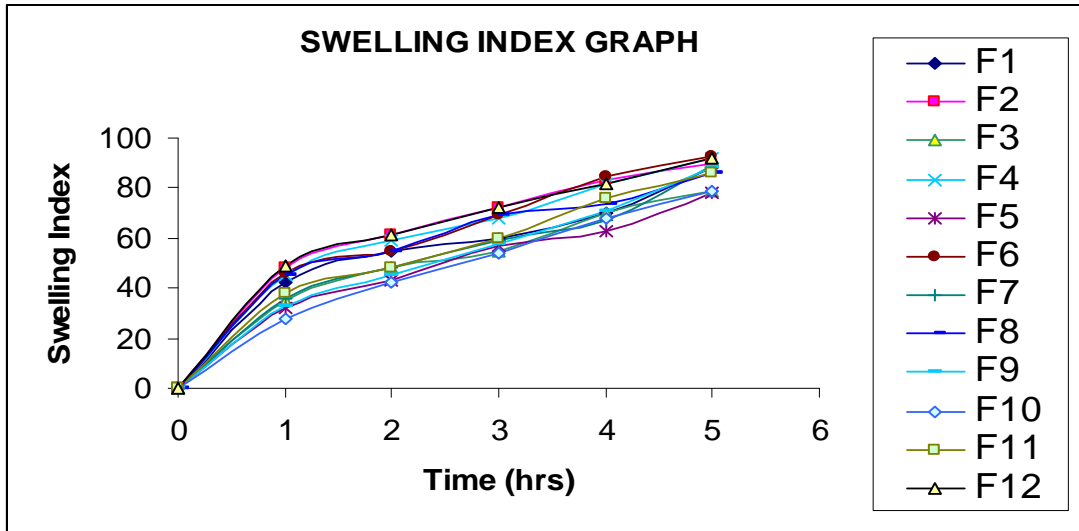


Fig. 2. Graph of swelling index v/s time (hrs)

Table 7. → Effect of hardness on Buoyancy Lag Time of formulation F6

Hardness in kg/cm <sup>2</sup>	Buoyancy Lag Time (sec)
4	85
5	132
6	168
7	230
8	300

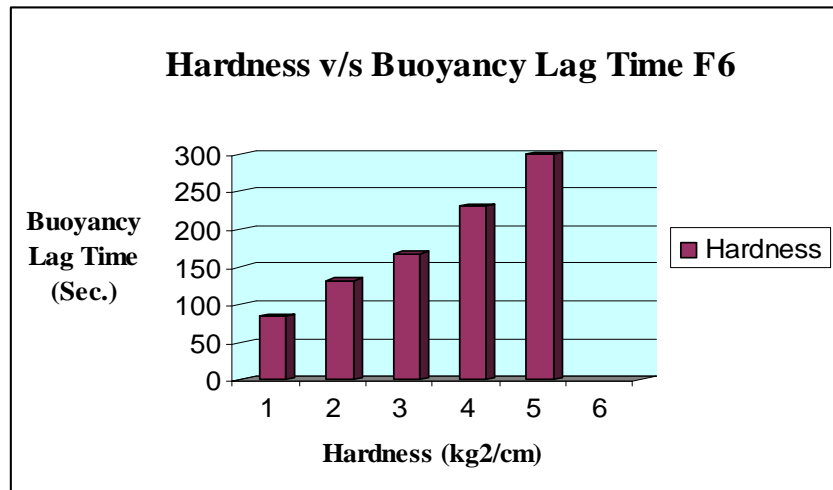
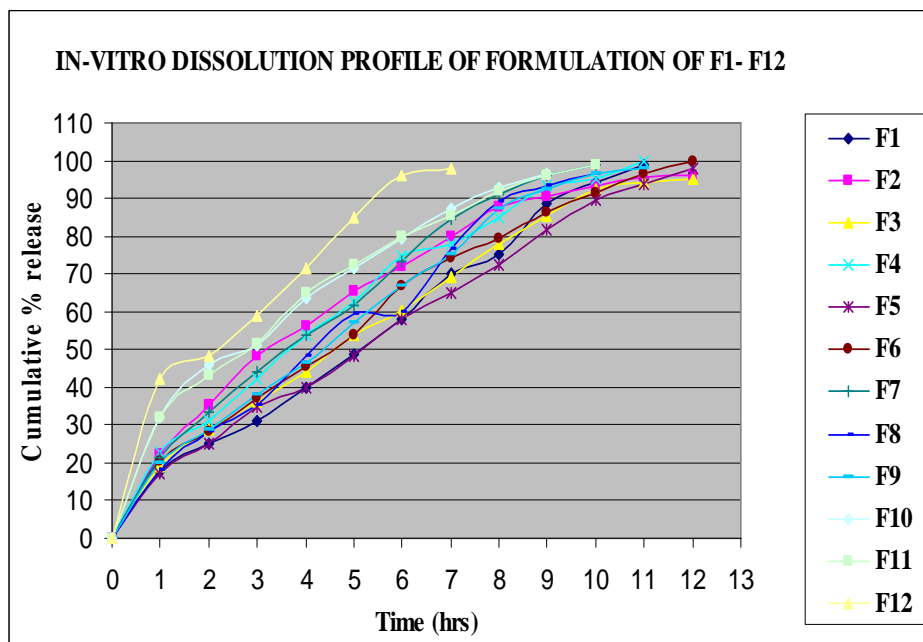


Fig. : 3 Plot of hardness v/s buoyancy lag time of f 6



**Figure 4: In-vitro dissolution profile of formulations F1 To F12**

## Conclusion

Recent scientific and patent literature shows increased interest in academics and industrial research groups regarding novel dosage forms that can be retained in the stomach for prolonged and predictable period of time and the most feasible approach for this is to control the gastric residence time using gastroretentive dosage forms which will provide new and important therapeutic option. But the problem can arise if there is a narrow window for drug absorption in the GIT or drug is unstable in the intestinal fluid. So the development of oral controlled dosage form is not just to prolong the drug release but also to ensure the presence of dosage form in the stomach or upper GIT so that drug is released and absorbed for the desired period of time. Controlling the residence of a drug delivery system in a particular region of the gastrointestinal tract, can utilize several approaches: intragastric floating systems, high density systems, mucoadhesive systems, magnetic systems, unfoldable, extended or expandable systems and superporous, biodegradable hydrogel systems. Diltiazem Hydrochloride is a calcium channel blocker belonging to the benzothiazepine family. It is widely prescribed for the treatment for hypertension and angina pectoris. It has an elimination half-life of 3-4.5 hours and has an absorption zone from the upper intestinal tract. The duration of antihypertension action and antianginal after a single oral dose of Diltiazem Hydrochloride is only 3-4 hrs, clinical use required a daily dose of 30mg, to be taken 3 to 4 time a day in order to maintain adequate plasma concentrations. Due to short half-life of Diltiazem Hydrochloride required frequent administration and Efficacy of the administered dose may get diminished to incomplete drug release from the device above the absorption zone. These two drawbacks can be overcome by developing a floating dosage form which remained buoyant in the stomach, increases the gastric retention time so that it remain in the acid environment until all the drug is released. IR studies of the prepared matrix tablets and the drug and the excipients showed that no polymorphic changes occurred during manufacturing of tablets as all the peaks were present in the IR graph of tablet

sample. Stability studies at room temperature, and 40<sup>0</sup>C, for one month, indicate that even at extreme conditions, no change in the physical appearance of the mixtures and the tablets was found. The decrease in percentage drug contents of the different formulation was found to be <1.0%.U.V. Scanning of Diltiazem Hydrochloride was preformed and the  $\lambda_{max}$  at 236.80nm was found to be the most appropriate for the determination of concentration of Unknown Samples. Standard curve of Diltiazem Hydrochloride was carried out at  $\lambda_{max}$  236.80nm. and the correlation was found to be 0.9993. From in-vitro drug dissolution studies of the different batches of Diltiazem Hydrochloride, it was observed that with increasing the viscosity and content of HPMC and low % of Ethylcellulose, the rate and extent of drug release from the tablets decreases. This is because, as the molecular weight of the HPMC increase, the degree of entanglement of polymer chain increases. Thus the mobility of the drug molecule in the fully swollen system decrease. The formulation F<sub>6</sub> which contains 10% of Ethylcellulose, HPMC K<sub>4</sub>M and HPMC K<sub>15</sub>M released 99.81% of drug at 12 hrs.From the in-vitro buoyancy studies, it was found that almost all the batches containing effervescent agent showed immediate buoyancy lag time followed by floating period of more than 12hr. Swelling study showed satisfactory results for all batches(F1-F12). From the results obtained, it was concluded that the formulation F<sub>6</sub> is the best formulations as the extent of drug release was found to be around 99.81 % at the desired time 12 hrs. This batch also show buoyancy lag time and floating duration of more than 12hrs..Thus it is summarized and concluded that HPMC K<sub>4</sub>M, HPMC K<sub>15</sub> M and ethyl cellulose can be successfully used in formulation of Diltiazem Hydrochloride sustained release gastro retentive floating drug delivery system using Hydrophilic and Hydrophobic polymer.

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