CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.23860323

Available online at: http://www.iajps.com Research Article

DEVELOPMENT AND IN VITRO EVALUATION OF FLOATING DRUG DELIVERY SYSTEM OF DILTIAZEM HYDROCHLORIDE

Dr. G. Sri Lakshmi[1], Mekala uday kiran[2], Arrolla Vaishnavi[2], Appanagari Varshini[2], Reddy pelli Venu[2], Pasham Venu[2], Zakiya sultana[2]

[1]Associate Professor, Department of Pharmaceutical chemistry, Teegala Ram Reddy college of pharmacy, Meerpet, Hyderabad, Ranga Reddy Telangana - 500097, India.

[2]Students, Teegala Ram Reddy college of pharmacy, Meerpet ,Hyderabad, Ranga Reddy Telangana - 500097, India.

Abstract:

The present study was undertaken to formulate and evaluate floating tablets of Diltiazem Hydrochloride for sustained drug release and prolonged gastric retention. FTIR studies revealed no significant interaction between the drug and excipients, indicating good compatibility. The powder blends exhibited satisfactory flow properties suitable for tablet compression. The prepared tablets showed acceptable hardness, thickness, friability, weight variation, and drug content values within pharmacopeial limits. Floating studies demonstrated that all formulations exhibited rapid buoyancy with floating lag times ranging from 42 to 49 seconds.In vitro dissolution studies revealed sustained drug release over a period of 8 hours. Among the developed formulations, F3 exhibited the highest cumulative drug release (97.83%) and the shortest floating lag time (42 seconds), indicating superior formulation performance. Accelerated stability studies conducted on the optimized formulation (F3) for 90 days under different storage conditions showed no significant changes in drug release characteristics, confirming the stability of the formulation.The results of the study suggest that the developed floating tablets of Diltiazem Hydrochloride provide effective gastroretentive behavior and sustained drug release. Therefore, the optimized formulation represents a promising gastroretentive drug delivery system that may enhance therapeutic efficacy, prolong gastric residence time, and improve patient compliance.

Keywords: *Diltiazem Hydrochloride, Floating Tablets, Gastroretentive Drug Delivery System, Ethyl Cellulose, Eudragit RS100, Sustained Release, In Vitro Drug Release, Stability Studies.*

Corresponding author:

Dr. G. Sri Lakshmi,

Associate professor, Department of Pharmaceutical chemistry, Teegala Ram Reddy College of Pharmacy, Hyderabad - 500097, Telangana, India.

Mobile:

Email Id:

QR CODE

Please cite this article in press ***G. Sri Lakshmi*** *et al.,* ***Development And In Vitro Evaluation Of Floating Drug Delivery System Of Diltiazem Hydrochloride.,****. Indo Am. J. P. Sci, 2026; 13(10).*

INTRODUCTION:

Oral drug delivery remains the most widely preferred route for drug administration because of its convenience, cost-effectiveness, high patient compliance, and ease of manufacturing. However, conventional oral dosage forms often exhibit limited therapeutic efficacy due to rapid gastric emptying, short gastrointestinal residence time, and incomplete drug absorption, particularly for drugs that are primarily absorbed in the upper gastrointestinal tract. These limitations have led to the development of advanced gastro-retentive drug delivery systems (GRDDS), which are designed to prolong gastric residence time, improve drug bioavailability, and provide sustained therapeutic effects. Among the various gastro-retentive approaches, Floating Drug Delivery Systems (FDDS) have gained considerable attention because of their ability to remain buoyant on gastric fluids for an extended period without affecting the normal rate of gastric emptying. These systems possess a bulk density lower than that of gastric fluid, allowing them to float in the stomach and gradually release the drug in a controlled manner. The prolonged gastric residence time enhances drug absorption, reduces dosing frequency, minimizes fluctuations in plasma drug concentration, and improves patient compliance. Floating systems are particularly beneficial for drugs that exhibit a narrow absorption window in the upper gastrointestinal tract, are unstable in the intestinal environment, or require local action in the stomach.Floating drug delivery systems are generally classified into effervescent and non-effervescent systems. Effervescent systems contain gas-generating agents such as sodium bicarbonate and citric acid, which produce carbon dioxide upon contact with gastric fluid. The generated gas becomes entrapped within the hydrated polymer matrix, decreasing the density of the dosage form and enabling it to float. Non-effervescent systems rely on swellable polymers such as hydroxypropyl methylcellulose (HPMC), sodium alginate, xanthan gum, and carbopol, which hydrate upon contact with gastric fluid to form a gel barrier that maintains buoyancy while controlling drug release. The choice of polymer and formulation composition significantly influences floating lag time, total floating duration, swelling behavior, and drug release kinetics.

Diltiazem Hydrochloride is a calcium channel blocker belonging to the benzothiazepine class and is widely prescribed for the management of hypertension, chronic stable angina, and certain cardiac arrhythmias. It inhibits the influx of calcium ions into cardiac and vascular smooth muscle cells, resulting in vasodilation, decreased myocardial oxygen demand, and improved coronary blood flow. Despite its therapeutic effectiveness, Diltiazem Hydrochloride exhibits a relatively short biological half-life of approximately 3–5 hours and requires multiple daily administrations when formulated as an immediate-release dosage form. Frequent dosing may reduce patient adherence and produce fluctuations in plasma drug concentrations.

The development of a floating drug delivery system for Diltiazem Hydrochloride offers an effective strategy to overcome these limitations. By prolonging gastric residence time and providing sustained drug release, the floating system can maintain therapeutic plasma concentrations over an extended period, reduce dosing frequency, improve patient compliance, and potentially enhance oral bioavailability. Furthermore, gastro-retentive formulations minimize fluctuations in drug concentration, thereby improving therapeutic efficacy and reducing adverse effects associated with peak plasma levels.

MATERIALS:

Diltiazem hydrochloride was procured from Synpharma Research Labs, HYD., Ethyl cellulose, Eudragit RS 100, Citric acid, Sodium bi carbonate, Magnesium stearate, Talc and Micro crystalline cellulose were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

METHODOLOGY:

Formulation development

Table-1: Composition Of Diltiazem Hydrochloride Floating Tablets

Ingredients (mg)	F1	F2	F3	F4
Diltiazem hcl	60	60	60	60
Ethyl cellulose	40	80	-	-
Eudragit RS 100	-	-	40	80
MCC	172	132	172	132
Citric acid	10	10	10	10

Sodium bi carbonate	15	15	15	15
Magnesium stearate	2	2	2	2
Talc	1	1	1	1
Total wt	300	300	300	300

Preparation of Formulation:
Different tablet formulations were prepared by direct compression method. The formulations are composed of natural polymers. All powders were passed through 40-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 300 mg.

Evaluation of tablets

Physical Appearance:

The general appearance of a tablet, its identity and general elegance is essential for consumer acceptance, for control of lot-to-lot uniformity and tablet-to-tablet uniformity. The control of general appearance involves the measurement of size, shape, colour, presence or absence of odour, taste etc.

Size & Shape:
It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by micro-meter or by another device. Tablet thickness should be controlled within a ± 5% variation of standard value.

Weight variation test:
Twenty tablets were weighed individually and the average weight was calculated. The individual tablet weights are then compared to the average weight. Not more than two tablets should differ in their average weight by more than percentages stated in USP. No tablet must differ by more than double the relevant percentage.

Content Uniformity:
Randomly select 30 tablets. 10 of these assayed individually. The Tablet pass the test if 9 of the 10 tablets must contain not less than 85% and not more than 115% of the labeled drug content and the 10th tablet may not contain less than 75% and more than 125% of the labeled content. If these conditions are not met, remaining 20 tablets assayed individually and none may fall outside of the 85 to 115% range.

Friability:
A number of tablets are weighed and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed and the weight compared with the initial weight. The loss due to abrasion is a measure of the tablet friability. The value is expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked.
The percentage friability was determined by the formula:

$$\% \text{ friability} = (W_1 - W_2) / W_1 \times 100$$

W_1 = Weight of tablets before test
W_2 = Weight of tablets after test

Floating lag time:
The time between the introduction of the tablet into the medium and its rise to upper one third of the dissolution vessel is termed as floating lag time and the time for which the dosage form floats is termed as the floating or flotation time. These tests are usually performed in simulated gastric fluid or 0.1NHCl maintained at 37 ^{0}C, by using USP dissolution apparatus containing 900 ml of 0.1N HCl as the dissolution medium.

Drug release studies:
The drug release from the diltiazem hydrochloride tablets was investigated in a USP-II (paddle) apparatus, 900 ml of 0.1N HCl (50 rpm, 37°C). At predetermined time intervals, 5-ml samples were withdrawn and take 1ml sample and diluted to 10 ml and then analyzed with UV spectrophotometry.

Stability studies:

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 diltiazem hydrochloride 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:

Pre-compression Parameters

Bulk Density: The bulk density for the formulated blend was carried out for all formulation and found in the range of 0.478-0.492.

Tapped density: The tapped density for the formulated blend was carried out for all formulation and found in the range of 0.581-0.587.

Angle of repose: The angle of repose for the formulated blend was carried out. It concludes that all the formulations blend was found to be in the range of 25^0 to 30^0

Compressibility index: Compressibility index was carried out, it found between 10% to 17.47 % indicating the powder blend have the required flow property for compression.

Hausner ratio: Hauser ratio was carried out, it found between 1.20 to 1.21 indicating the powder blend have the required flow property for compression.

Table-2: Evaluation parameters of diltiazem hydrochloride

S. no	Bulk density	Tapped density	Compressibility index	Hausner ratio	Angle of repose (0)
F1	0.492	0.587	15.62	1.20	30^0
F2	0.478	0.581	17.47	1.21	25^0
F3	0.484	0.582	16.83	1.20	27^0
F4	0.490	0.585	16.15	1.21	29^0

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-3: Evaluation parameters of diltiazem HCL floating tablets

Parameter	F1	F2	F3	F4
Weight variation	300	299	300	301
Thickness (mm)	2.7	2.6	2.8	2.2
Hardness (kg/cm^2)	4.1	4.3	4.8	4.1
Friability	0.25	0.30	0.27	0.31
Content uniformity	82.69	85.12	91.52	81.25
Floating lag time (Sec)	43	49	42	47

Floating lag time

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 F3 was 42 sec.

In vitro Dissolution studies

The dissolution conditions used for studying the drug release from tablet of diltiazem hydrochloride are:

Apparatus : USP apparatus II (Paddle)
Agitation speed (rpm) : 50rpm
Medium : 0.1N HCl
Volume : 900 ml
Temperature : 37.0 ± 0.5 C
Time : 1,2,3,4,5,6,7 and 8hrs.
Wavelength : 236 nm

The samples were withdrawn at predetermined time points, and were analyzed spectrophotometrically at 236 nm.

Table-4: In vitro drug release of diltiazem hydrochloride floating tablets

Time	F1	F2	F3	F4
0	0	0	0	0
1	18.41	17.85	19.13	18.14
2	36.93	35.46	34.56	32.10
3	47.86	45.17	44.25	42.10
4	58.46	55.43	59.60	55.18
5	67.86	66.50	69.52	67.25
6	78.42	77.86	79.82	72.18
7	85.10	84.25	86.15	85.20
8	94.68	95.52	97.83	96.39

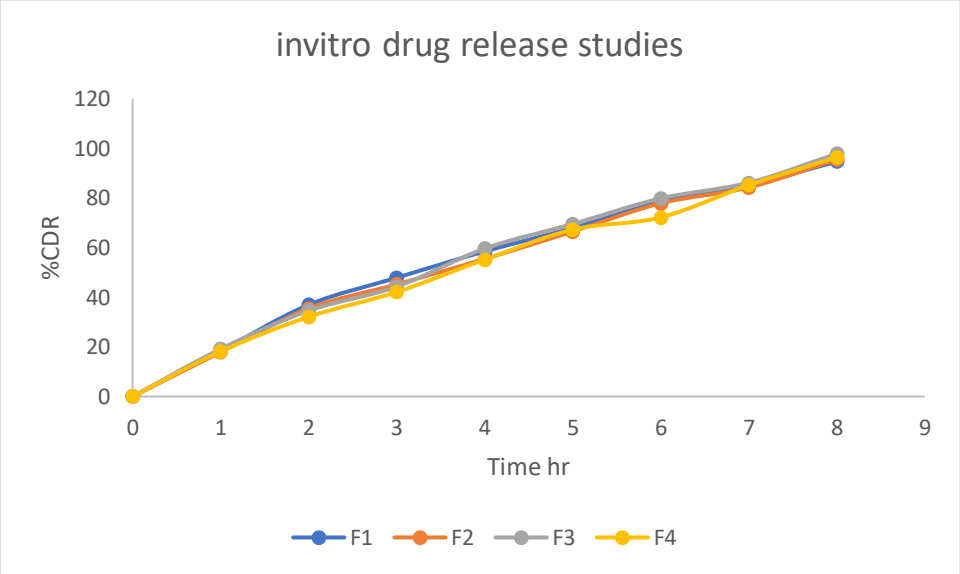


Fig-1: In vitro drug release for all the formulations

Stability Study

There was no significant change in physical and chemical properties of the tablets of formulation F-3 after 90 days. Parameters quantified at various time intervals were shown. Optimized formulations F3 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-5: Stability study for optimized formulation

Formulation Code	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-3	**25^{0}C/60%RH % Release**	97.83	96.25	95.26	94.15	**Not less than 85 %**
F-3	**30^{0}C/75% RH % Release**	97.83	96.18	95.27	94.19	**Not less than 85 %**
F-3	**40^{0}C/75% RH % Release**	97.83	96.10	95.23	94.25	**Not less than 85 %**

SUMMARY & CONCLUSION:

The present study was undertaken to formulate and evaluate floating tablets of Diltiazem Hydrochloride using Ethyl Cellulose and Eudragit RS100 as release-retarding polymers.Preformulation studies confirmed the suitability of Diltiazem Hydrochloride for formulation development. The powder blends exhibited satisfactory flow properties with bulk density ranging from 0.478–0.492 g/cm³, compressibility index ranging from 15.62–17.47%, Hausner ratio between 1.20–1.21, and angle of repose between 25° and 30°.The prepared tablets showed acceptable physical characteristics, including hardness, thickness, friability, weight variation, and drug content. Floating studies demonstrated that all formulations exhibited floating behavior with lag times ranging from 42 to 49 seconds.In vitro dissolution studies showed sustained drug release over 8 hours. Among all formulations, F3 exhibited the highest cumulative drug release (97.83%) along with the shortest floating lag time (42 sec), indicating superior formulation performance.Accelerated stability studies conducted on the optimized formulation F3 for 90 days under different storage conditions showed no significant changes in drug release characteristics, confirming the stability of the formulation.Floating tablets of Diltiazem Hydrochloride were successfully formulated using Ethyl Cellulose and Eudragit RS100 by the direct compression method. The prepared formulations demonstrated satisfactory pre-compression and post-compression characteristics, good floating behavior, and sustained drug release properties.

Among all the formulations, F3 was identified as the optimized formulation based on its desirable floating lag time (42 sec), highest cumulative drug release (97.83%), acceptable tablet properties, and good stability profile. FTIR studies confirmed the compatibility of Diltiazem Hydrochloride with the selected excipients, while stability studies demonstrated that the optimized formulation remained stable under accelerated storage conditions.

REFERENCES:

1. Bagherwal A, Patidar DK, Sharma P. Formulation and evaluation of floating tablets of ciprofloxacin hydrochloride. Int J Comp Pharma 2010;1:1-4.
2. Kumar R. Development and *in-vitro* evaluation of sustained release floating matrix tablets of metformin hydrochloride. Int J Pharm Sci Res 2010;1:96-101.
3. Chodavarapu NP, Yendluri RB, Suryadevara H, Reddy P, Chhatoi P. Formulation and evaluation of abelmoschusesculentus mucilage based metformin hydrochloride floating matrix tablets. Int J Pharm Tech 2011;3:2725-45.
4. Kshirsagar RV, Jain V, Wattamwar S. Effect of different viscocity grade HPMC polymer on gastroretantive drug delivery of metformin hydrochloride. Int J Appl Pharm 2009; 1:44-50.
5. Chandiran IS, Kumar BP, Narayan V. Formulation and *in-vitro* evaluation of floating drug delivery system for salbutamol sulphate. Int J Pharm Biomed Sci 2010; 1(1):12-15.
6. Hu L, Li L, Yang X, Liu W, Yang J, Jia Y, *et al.,* Floating matrix dosage form for dextromethorphan hydrobromide based on gas forming technique. *In-vitro* and *in-vivo*evalvation healthy volunteers. Eur J Pharm Sci 2011;42:99-105.
7. Raju BD, Sreenivas R, Varma MM. Formulation and evaluation of floating drug delivery system of metformin hydrochloride. J Chem Pharm Res 2010;2(2):274-78.
8. Senthilkumar SK, Jaykar B, Kavimani S. Formulation and evaluation of gastroretentive floating drug delivery system of rabeprazole sodium. Int J Biopharm 2011;2(2):57-62.
9. Mohammed MS. Formulation and *in-vitro* evaluation of sustained release intragastric tablets of propranolol hydrochloride using natural polymer. J Pharm Biomed Sci 2011;10(10):1-10.
10. Goole J, Vanderbist F, Amighi K. Development and evaluation of new multi-unit levodopa sustained-release floating dosage forms. Ind J Pharm 2007;334:35-41.

11. Sauzet C, Bruno CM, Nicolas M, Kister J, Piccerdle P, Prinderre P. An innovative floating gastro retentive dosage system. Formulation and *in-vitro* evaluation. Int J Pharm 2009;378:23-29.
12. Abrahamsson, B., Alpsten, M., Hugosson, M., Jonsson, U.E., Sundgren, M., Svenheden, A., Tölli, J., 1993. Absorption, Gastrointestinal Transit, and Tablet Erosion of Felodipine Extended-Release (ER) Tablets. Pharm. Res. 10, 709-714.
13. Agrawal, A.M., Manek, R.V., Kolling, W.M., Neau, S.H., 2003. Studies on the interaction of water with ethylcellulose: effect of polymer particle size. AAPS Pharm. Sci. Tech. 4, E60.
14. Alvisi, V., Gasparetto, A., Dentale, A., Heras, H., Felletti-Spadazzi, A., D'Ambrosi, A., 1996. Bioavailability of a controlled release formulation of ursodeoxycholic acid in man. Drugs Exp. Clin. Res. 22, 29-33.
15. Amaral, M.H., Lobo, J.M., Ferreira, D.C., 2001. Effect of hydroxypropyl methylcellulose and hydrogenated castor oil on naproxen release from sustained-release tablets. AAPS Pharm. Sci. Tech. 2, E6.
16. Andrews, G.P., Laverty, T.P., Jones, D.S., 2009. Mucoadhesive polymeric platforms for controlled drug delivery. Eur. J. Pharm. Biopharm. 71, 505-518.