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Formulation, In-Vitro Evaluation of Flupirtine Floating Tablets Using Different Polymers

Middela Karthik, Ph. D Research SCHOLAR, Department of Pharmacy, Shri JJT University Jhunjhunu, Rajasthan, India
Email: Karthik.middela@gmail.com
Dr. Ankit Singh, Research Guide, Department of Pharmacy, Shri JJT University, Jhunjhunu, Rajasthan, India
Dr. P Raja Sridhar Rao, Research Co- Guide, Department of Pharmacy, Shri JJT University, Jhunjhunu, Rajasthan, India

Abstract

The main objective of this study was to develop and evaluate floating tablets of flupirtine using the polymers HPMC K4M, Eudragit RS 100, and Eudragit RL 100 through direct compression. Nine different formulations of flupirtine were created and analyzed. No incompatibilities were found, and the pre-compression assessments for all formulations exhibited good flow characteristics. The post-compression evaluations met the acceptable standards for each formulation. Among the formulations, F5, which included Eudragit RS 100, achieved the highest drug content of 95.27% over a period of 12 hours, designating it as the optimized formulation. Kinetic analysis revealed that the optimized formulation F5 exhibited non-Fickian release behavior. Stability tests for formulation F5 indicated that the drug remained stable for six months under the specified conditions, with all parameter results considered satisfactory.

Keywords: Flupirtine, HPMC K4M ,Eudragit RS 100 and Eudragit RL 100, buoyancy, Invitro drug release, stability study.

INTRODUCTION

Oral drug delivery is the preferred administration method due to its ease of use and high patient compliance. Dosage forms have evolved from immediate-release to site-specific delivery systems. The main goal of any drug delivery system is to ensure that the therapeutic dose reaches its target site effectively and maintains the desired concentration. Gastroretentive drug delivery systems (GRDDS) enhance medication bioavailability by extending gastric residence time and enabling site-specific release. Floating drug delivery systems, a type of GRDDS, have gained attention for their ability to remain buoyant in gastric fluid, prolonging drug release at optimal absorption sites. Flupirtine is a non-opioid pain reliever with muscle relaxant effects, used primarily for musculoskeletal pain. Unlike NSAIDs, it works by inhibiting pain signals and reducing neuronal excitability, providing a well-tolerated alternative to opioids and NSAIDs.

Chemicals and Reagents:

Flupirtine was provided by Aurobindo Pharma Ltd. Dicalcium Phosphate and Carnauba wax came from Dr. Reddy's Laboratories. HPMC K4M, Eudragit RS-100, Eudragit RL-100, Talc, and Sodium Bicarbonate were sourced from SD Fine Chemicals Pvt Ltd, while Citric Acid was obtained from Ajantha Chemicals. Magnesium stearate was supplied by Qualikems Fine Chemicals.

Preformulation Studies

Preformulation testing is the first step in developing drug dosage forms. It examines the physical and chemical properties of the drug, both alone and with excipients. The goal is to gather essential information for creating stable and bioavailable formulations.

Identification of Pure Drug:

Flupirtine was identified utilizing Infrared Absorption Spectroscopy.

Melting Point Determination:

The melting point of Flupirtine was assessed using the open capillary method.

Solubility Studies:

Solubility is a crucial physicochemical parameter for a drug, as it influences bioavailability, the rate of drug release into the dissolution medium, and ultimately, the therapeutic efficacy of the pharmaceutical product. To evaluate the solubility of Flupirtine, the equilibrium solubility method was employed. In this method, an excess quantity of the drug is placed in 10 ml of

solvent within a conical flask, which is then placed on a rotary shaker. The flask is shaken at a speed of 100 rpm for 24 hours. Following this, the solution is filtered, and the absorbance is measured using a UV-visible spectrophotometer to determine the concentration. The solvents used in these solubility studies included water and 0.1N HCl.

Drug-Excipient Compatibility Studies:

A stable and effective solid dosage form depends on selecting the right excipients, which aid in administration, ensure consistent drug release and bioavailability, and protect the drug from degradation. Compatibility studies are essential when using new excipients with an active substance. The compatibility of Flupirtine with various polymers and excipients was assessed using Fourier Transform Infrared Absorption (FTIR) analysis.

Flow Properties

Angle of Repose:

The angle of repose is the maximum angle between a pile of powder and a horizontal plane, used to assess flow characteristics. Poor powder flow results from frictional forces between particles, which the angle of repose quantifies.

The angle of repose (θ) was elegantly determined using the following formula:

$$\text{Tan } \theta = h / r$$

$$\theta = \text{tan-1 } (h/r)$$

Tan θ = height of pile in cm/ radius of pile in cm

θ = tan-1 (height of pile in cm/ radius of pile in cm)

Bulk density:

Bulk density is defined as the ratio of the total mass of a powder to its bulk volume. It is mathematically represented as follows:

$$Db = \text{Mass /bulk volume}$$

Bulk density is measured using a bulk density apparatus. A sample of 50 g of powder is added to a 100 ml graduated cylinder, which is then tapped 100 times. The final volume occupied by the powder is recorded and used to calculate the bulk density.

Tapped density:

The procedure involved placing a graduated cylinder filled with a known mass of a drug-excipient blend onto a mechanical tapping apparatus. The tapped volume was determined by tapping the powder until a constant volume was achieved. This volume is expressed in grams per milliliter (g/ml).

Tapped density = M/Vt

Where

M= mass of powder and

Vt= tapped volume of the powder.

Compressibility Index (Carr's Consolidation Index):

One method for measuring free-flowing powder is compressibility, calculated from the powder's density using a specific formula.

Percentage Compressibility = [Tapped density-bulk density/tapped density] x 100

Hausner's Ratio:

Hausner's ratio is an indirect measure of powder flow ease. If the Hausner's ratio of a powder is close to 1.25, it indicates better powder flow. It is calculated using the following formula.

= Dt / Db

Where, Db represents the bulk density of the powder, and Dt represents the tapped density of the powder.

Calibration Curve for Flupirtine in 0.1 N HCl

Preparation of 0.1 N HCl:

Dilute 8.5 mL of concentrated hydrochloric acid in 1000 mL of distilled water.

Preparation of 0.5% SLS Solution (pH 1.2):

Dissolve 5 g of sodium lauryl sulfate in 1000 mL of 0.1 N HCl and adjust the pH if necessary.

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Flupirtine Stock Solution:
Dissolve 50 mg of flupirtine in 100 mL of 0.1 N HCl to create a 500 µg/mL solution.
Method:
Dilute aliquots of the stock solution to obtain concentrations of 5, 10, 15, 20, and 25 µg/mL. Measure absorbance between 200 and 400 nm, noting maximum absorbance at 245 nm (λmax).
Calibration Curve Procedure:
Allow standards to stand for 5 minutes at λmax. Measure absorbance against a solvent blank and plot absorbance versus concentration to create a calibration curve.
Preparation of Flupirtine Gastro-Retentive Floating Tablets
The gas-generating floating tablets of Flupirtine were manufactured using a direct compression method. All polymers, the drug, and excipients were passed through a sieve with a mesh size of 40 before being used in the formulation.
Steps involved in the manufacture of the tablets:
1. The drug, polymers, and other excipients were passed through a 40-mesh sieve.
2. The required quantities of the drug, polymers, and excipients were weighed accurately and transferred into a polyethylene bag, where the blend was mixed for at least 15 minutes.
3. The blend was then lubricated by adding different concentrations of magnesium stearate and 1.5% talc, followed by an additional 5 minutes of mixing.
4. The tablets were compressed using 12 mm diameter punches in an 8-station Cadmac tablet punching machine.

Table Design of Formulation chart of F1-F9
Evaluation of prepared Tablets

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Flupirtine	50	50	50	50	50	**50**	50	50	50
Di-calcium phosphate	133	130	127	133	130	127	133	130	127
Carnauba wax	30	30	30	30	30	30	30	30	30
HPMC K4M	3	6	9	***	***	***	***	***	***
Eudragit RS 100	***	***	***	3	6	9	***	***	***
Eudragit RL 100	***	***	***	***	***	***	3	6	9
Sodium bi carbonate	50	50	50	50	50	50	50	50	50
Citric acid	25	25	25	25	25	25	25	25	25
Magnesium stearate	3	6	9	3	6	9	3	6	9
Talc	6	6	6	6	6	6	6	6	6
Total weight of tablet /mg	300	300	300	300	300	300	300	300	300

Weight Variation Test
Twenty tablets were randomly selected and accurately weighed. The average weight of the tablets was calculated, and each individual tablet's weight was compared to this average to determine the weight deviation. The results are expressed as mean values ± standard deviation (SD).
Friability
I weighed five tablets (W1) and placed them in the drum's end cover. After 25 rotations per minute (rpm), I reweighed them (W2) to determine the percentage loss.Weight loss, a measure of friability.

$$\% \text{ weight loss} = \frac{W1-W2}{W1} \times 100$$

Hardness
I assessed the hardness of three tablets from different preparations using the Monsanto hardness tester. After applying ten constant forces to each tablet until they fractured, I recorded the hardness scores and calculated the mean value and standard deviation to evaluate product consistency.

Thickness

Ten tablets were selected randomly from each formula and thicknesses were measured using Vernier caliper.

Determination of Drug Content in Tablet Formulation

Twenty tablets were powdered, and an amount equivalent to 300 mg of Flupirtine was transferred to a 100 mL volumetric flask with 0.1N HCl. After sonication for 30 minutes and filtration, the solution was diluted to the desired concentration. The absorbance was measured at 245 nm against a blank of 0.1N HCl. To ensure accuracy and precision, a standard additions technique was also employed.

In Vitro Buoyancy Studies

In vitro buoyancy studies evaluate the performance of floating tablet formulations through two main parameters: buoyancy lag time and floating duration time.

Buoyancy Lag Time: Tablets are dropped into a beaker with 200 mL of 0.1N HCl, and the time taken for them to rise to the surface is recorded. A shorter lag time indicates better buoyancy.

Floating Duration Time: Tablets are placed in the same beaker, and the time they remain on the surface is noted. Longer floating times suggest improved drug release and effectiveness.These studies are vital for understanding the sustained drug delivery potential of formulations.

Swelling index (SI)

In 0.1 N HCl at 37 ± 0.5°C weighed tablet was kept for some time. Excess liquid was removed, and the swelled reweighed tablet (W2).

To calculate

$$SI = \frac{W2-W1}{W1} \times 100$$

In-vitro drug release studies

Apparatus: USP dissolution apparatus II (paddle method, Electrolab)

Dissolution medium: 0.1 N HCl, 50 rpm and 37±0.50°C with a 900 ml.

Drug release was tested in 0.1 N HCl (pH 1.2), with samples collected at prescribed time interval. The release for Flupirtine was scored by UV-visible spectrophotometer at 249 nm.

9. Stability studies

Stability studies were conducted following ICH and WHO guidelines. Floating tablets were stored at40°C ± 20°C/ 75% ± 5% RH for 3 months.

10. Kinetics

Kinetics have been analyzed using model-dependent methods based on various mathematical functions to portray the dissolution profile.

Zero order models

According to zero-order models, accurately represented

Qt = K0t

Keep in mind that Qt represents the Portion of active substance dissolved at time t, and K0 is the

release constant. Optimized formulation data was plotted to study release kinetics.

First order model

The equation expresses the release of the drug, which operates according to first-order kinetics.

Log F = K1t

Remember, F symbolizes a discrete unit of drug release at time t, while K1 denotes the first-order release constant. The data we've collected is presented as a logarithmic plot of the remaining drug's cumulative percentage against time.

Higuchi model

The data obtained were plotted as the cumulative percentage of drug release versus the square root of time, using Equation (10) to determine release kinetics.

Qt = KH t1/2
Qt is the count of the drug dissolved at time t,
KH is the Higuchi dissolution constant.

Korsemeyer-Peppas model

Kinetics study, release data were plotted as the cube root of drug percentage remaining in the matrix versus time, expressed by

$M^t / M^\infty = K\ t^n$

Where, M_t is represents amount of the released drug at time t,
M_∞ is the overall amount of drug released after 12 hrs,
K is the release rate constant
n is the release exponent/ diffusional exponent.

Dissolution Profile Comparison Using Similarity Factor, f2

Recently, the FDA has focused more on comparing dissolution profiles for post-approval changes and biowaivers. A dissolution profile provides a more accurate characterization of a product than a single-point test. Comparing profiles between pre-change and post-change products, especially for SUPAC-related changes or different strengths, ensures similar product performance and can indicate bioinequivalence. The f2 method is one of the simplest ways to compare dissolution profiles. Moore and Flanner proposed a model-independent approach using factors f1 and f2. The f2 formula is:

f2= 50+log [{1+(Rt-Tt)*1/n}-0.5]

Here, (Rt) and (Tt) are the cumulative percentage dissolved at selected time points for the reference and test products, respectively.

RESULTS AND DISCUSSION

Preformulation studies:

Identification of Flupirtine by FTIR studies:

Table: Characteristic absorption band frequency of Flupirtine

S. No	Name of the Compound	Functional Group Assigned (wave number in cm^{-1})				
		C-H stretching	C-C stretching	C=O stretching	O-H stretching	CH bending
S. No	Characteristic peak	2400-3600	1620-1700	1600-1900	3000-3700	1200-1550
01	Pure Flupirtine	2935.07 and 1132.41	1590.18	1647.59 and C-O-C stretching 1187.03	3556.07	1234.09
02	Drug+ HPMC K4M	2861.04	1687.04	1773.09	3534.12	1452.06
03	Drug+ Eudragit-RS 100	29540.78	1452.01	1812.07	3632.07	1444.08
04	Drug+ Eudragit-RL 100	2987.04	15970.36	1702.14	3412.04	1462.01
05	Drug+ excipient mixture	3485.01	1739.18	1765.01	3758.27	1524.07

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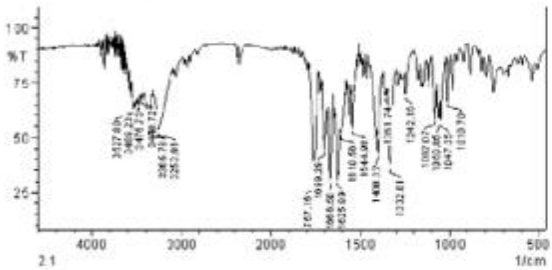
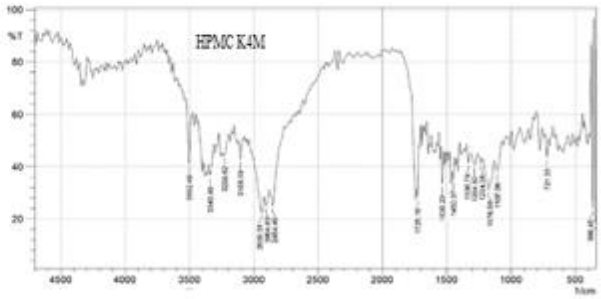
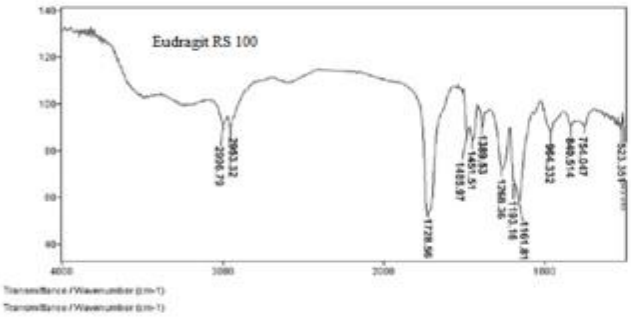


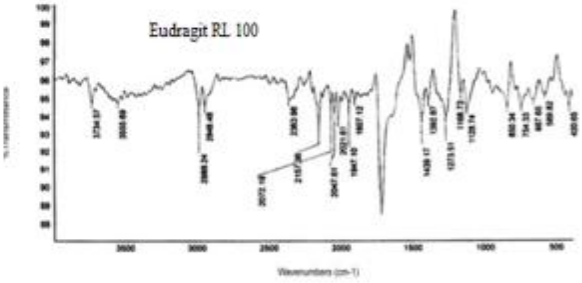
FTIR SPECTRUM OF HPMC K4 M



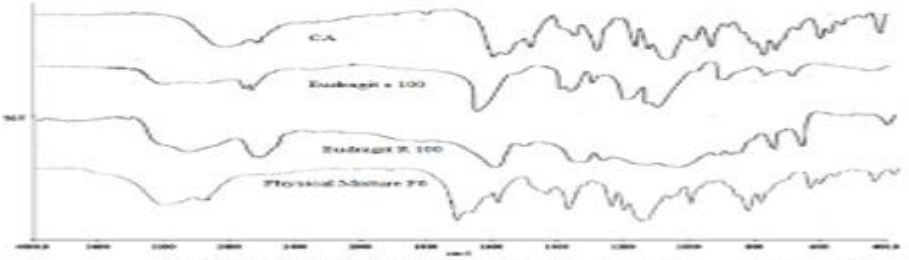
FTIR SPECTRUM OF PURE FLUPIRTINE



FTIR SPECTRUM OF EUDRAGIT RL 100



FTIR SPECTRUM OF EUDRAGIT RS 100



FTIR SPECTRUM OF Optimized Formulation F5

Analytical method for Flupirtine

Calibration curves for Flupirtine were established in a 0.1N HCl medium to accurately quantify the samples. All solutions were freshly prepared prior to use to ensure reliability and precision in the measurements. This approach allows for consistent and accurate assessment of Flupirtine concentration in the tested samples.

Table Standard calibration curve of Flupirtine at 245nm in 0.1 N HCl

Concentration µg/ml	Absorbance			Mean ± S.D
	I	II	III	
2	0.131	0.130	0.132	0.131±0.006
4	0.262	0.261	0.263	0.262±0.002
6	0.393	0.394	0.392	0.393±0.007
8	0.489	0.488	0.490	0.489±0.009
10	0.599	0.598	0.597	0.599±0.001
12	0.688	0.687	0.689	0.688±0.003
14	0.784	0.785	0.783	0.784±0.005
16	0.893	0.893	0.892	0.893±0.006
18	0.987	0.988	0.986	0.987±0.004
20	1.212	1.0211	1.213	1.212±0.002

(n=3)

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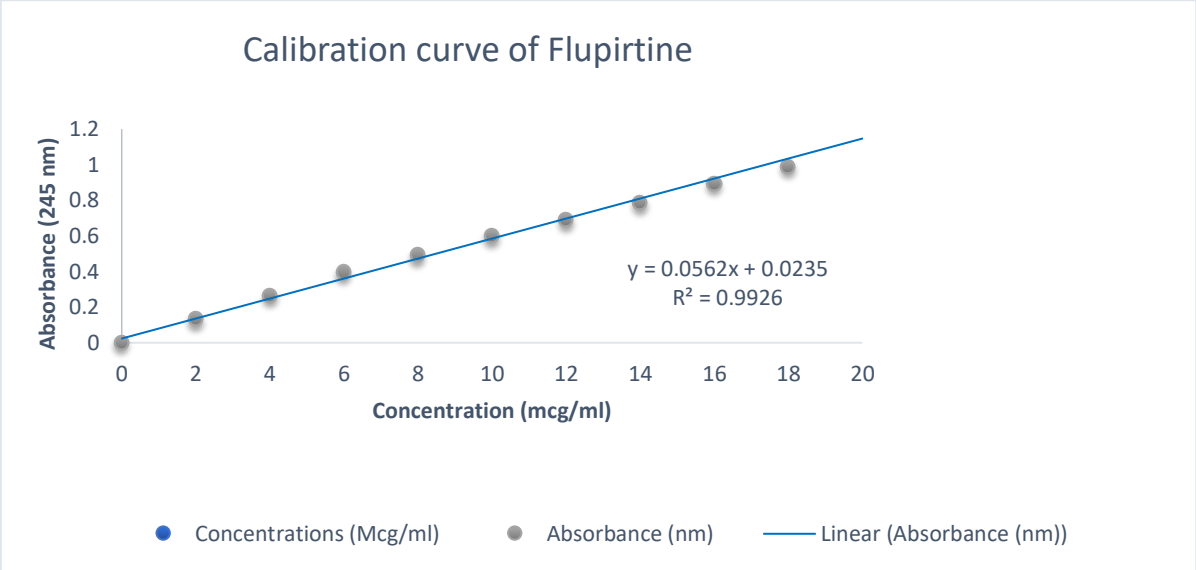
Figure: Standard calibration curve of Flupirtine at 245 nm in 0.1 N HCl



Pre-compression parameters

Table Evaluation of Flupirtine pre-compressional parameters

Code	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Hausner's ratio (H_R)	Carr Index (I_C)	Angle of Repose (θ)
F1	0.369±0.034	0.420±0.021	1.15±0.514	12.28±0.258	27.26±0.147
F2	0.325±0.028	0.412±0.026	1.19±0.828	12.23±0.321	30.27±0.258
F3	0.385±0.027	0.432±0.019	1.17±0.112	12.62±0.159	28.19±0.369
F4	0.391±0.068	0.418±0.027	1.12±0.584	13.24±1.147	29.67±0.159
F5	0.368±0.2.05	0.409±0.031	1.14±0.342	11.28±0.258	28.37±0.357
F6	0.394±0.079	0.461±0.014	1.16±0.458	12.34±0.357	26.18±0.456
F7	0.427±0.076	0.485±0.019	1.18±0.472	13.31±0.856	30.27±0.481
F8	0.388±0.079	0.427±0.028	1.17±0.420	14.39±1.651	31.16±0.174
F9	0.467±0.059	0.429±0.049	1.15±0.152	12.27±1.158	27.34±0.285

POST COMPRESSION PARAMETERS

Post- compressional parameters of Flupirtine Floating Tablets

Formulation code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight variation (mg)	Drug content (%)
F1	4.17±0.059	5.27±0.213	0.51±0.004	300.1±1.25	99.58±0.102
F2	4.27±0.047	5.23±0.312	0.46±0.025	301.3±1.24	98.09±0.120
F3	4.31±0.036	5.24±0.384	0.57±0.032	300.6±1.27	98.47±0.410
F4	4.29±0.078	5.22±0.554	0.55±0.042	300.5±1.26	98.83±0.511
F5	4.19±0.084	5.10±0.421	0.52±0.052	300.4±1.21	99.47±0.154
F6	4.18±0.067	5.23±0.748	0.53±0.062	300.9±2.14	99.65±0.451
F7	4.20±0.049	5.24±0.254	0.56±0.095	300.4±1.16	99.74±0.117
F8	4.25±0.076	5.17±0.016	0.53±0.042	300.3±1.26	98.46±0.801
F9	4.22±0.058	5.19±0.368	0.59±0.013	300.7±2.24	98.70±0.258

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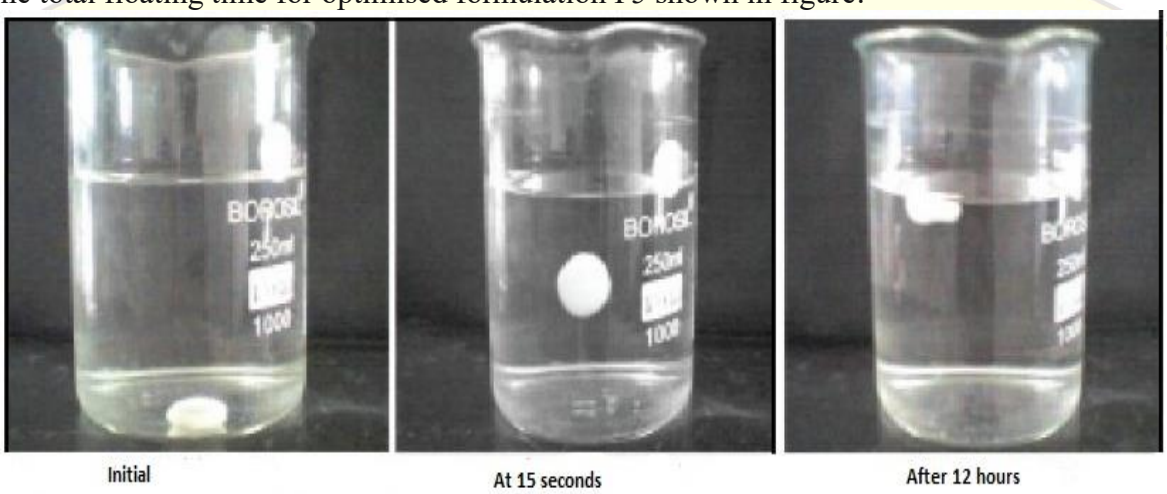
Table Post- compressional parameters of Flupirtine Floating Tablets

Formulation code	Swelling index (SI)	Buoyancy lag time (seconds)	Total floating time (hrs.)
F1	2.18±0.174	20.46±1.41	12
F2	3.58±0.067	24.15±1.45	12
F3	6.78±0.059	28.26±1.59	12
F4	2.05±0.137	19.37±2.41	12
F5	3.21±0.247	21.49±1.75	12
F6	6.17±0.156	26.17±2.84	12
F7	3.73±0.059	21.53±1.75	12
F8	3.75±0.257	25.64±1.57	12
F9	6.45±0.028	32.45±1.28	12

The total floating time for optimised formulation F5 shown in figure:



Initial At 15 seconds After 12 hours

Table: Dissolution profile of F1, F2 and F3

Time (hrs.)	F1	F2	F3
0	0	0	0
0.5	7.725±0.707107	7.9±0.014142	7.545±0.813173
1	16.235±1.421285	17.74±0.707107	16.105±1.039447
2	26.275±1.562706	29.76±0.551543	24.005±2.595082
3	38.38±1.697056	40.83±0.777817	35.065±0.106066
4	48.645±1.506137	53.105±0.516188	43.14±0.608112
6	57.355±1.718269	61.21±1.315219	51.465±1.011163
8	66.175±1.421285	69.105±0.516188	61.365±0.120208
10	74.23±1.527351	74.715±0.615183	67.715±0.784889
12	78.5±1.244508	85.865±0.360624	73.36±0.169706

Figure: Dissolution profile of F1, F2 and F3

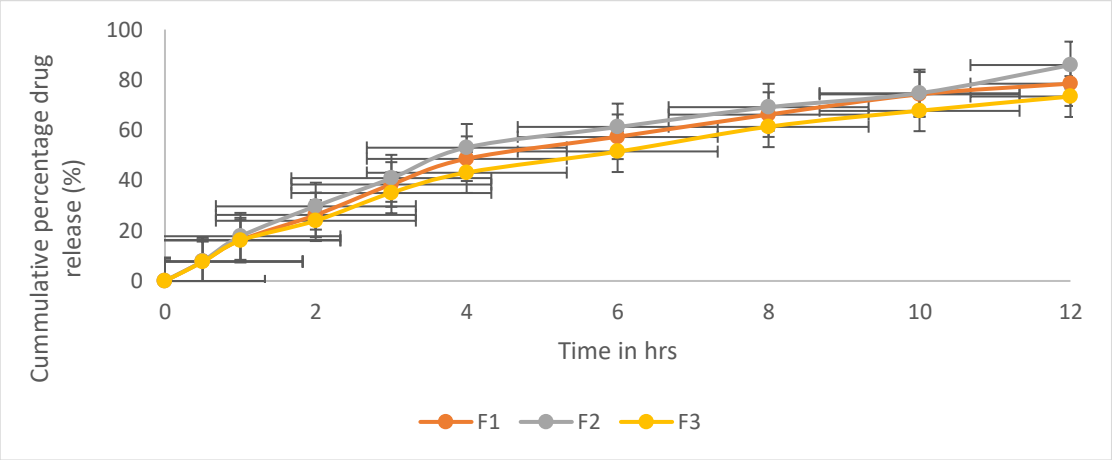


Table: Dissolution profile of F4, F5 and F6 and F6

Time (hrs.)	F4	F5	F6
0	0	0	0
0.5	9.725±0.26163	10.16±0.014142	8.625±0.304056
1	18.37±0.141421	24.785±0.841457	16.61±0.0480833
2	27.92±0.084853	34.92±0.777817	25.485±0.007071
3	37.375±0.756604	45.125±0.360624	33.075±0.714178
4	47.39±0.070711	55.115±0.502046	42.025±1.039447
6	53.68±0.0721249	64.78±0.692965	50.45±0.39598
8	61.985±0.629325	74.735±0.629325	58.925±0.714178
10	70.16±0.028284	85.715±0.643467	63.83±0.59397
12	80.335±0.13435	95.27±1.414214	72.36±0.39598

Figure: Dissolution profile of F4, F5

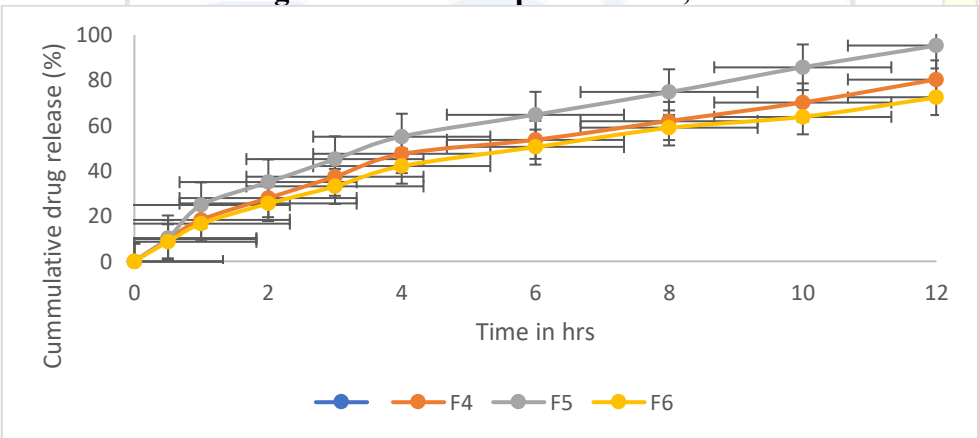


Table: Dissolution profile of F7, F8 and F9

Time (hrs.)	F7	F8	F9
0	0	0	0
0.5	9 ±0.141421	8.475±0.007071	7.4±0.070711
1	17.735±0.784889	17.16±0.452548	16.875±0.53033
2	26.88±0.848528	26.155±0.586899	26.035±0.784889
3	35.815±0.940452	35.16±0.452548	35.02±0.636396
4	44.965±1.1243	43.725±0.784889	43.73±0.777817
6	54.035±1.067731	53.83±0.509117	53.725±0.643467
8	63.445±0.388909	63.72±0.636396	63.11±0.509117

10	69.06±0.452548	74.035±0.784889	68.675±0.700036
12	76.935±0.502046	84.24±0.678823	74.88±0.438406

Figure: Dissolution profile of F7, F8 and F9

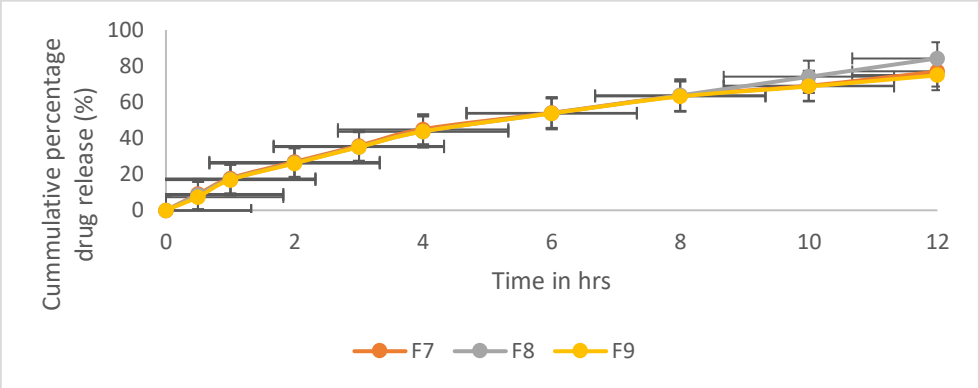


Table: Drug release kinetic models of Flupirtine floating tablets

Formulation code	Zero order (R^2)	First order (R^2)	Higuchi's plot (R^2)	Korsmeyer 'plot		Type of mechanism of drug release
				(R^2)	n	
F1	0.923	0.9921	0.9857	0.6437	0.937	Super case II transport
F2	0.831	0.9827	0.9847	0.9512	0.920	Super case II transport
F3	0.934	0.9922	0.9895	0.6403	0.931	Super case II transport
F4	0.935	0.9854	0.9919	0.5925	0.824	Non-Fickian type of release
F5	0.932	0.9466	0.9933	0.5767	0.696	Non-Fickian type of release
F6	0.935	0.9895	0.9931	0.6107	0.642	Non-Fickian type of release
F7	0.934	0.9934	0.9929	0.6075	0.710	Non-Fickian type of release
F8	0.963	0.9845	0.9888	0.6322	0.732	Non-Fickian type of release
F9	0.932	0.9927	0.9903	0.6378	0.732	Non-Fickian type of release

Table: Stability data for optimized formulation of Flupirtine Floating Tablet-F5

Name of Test	**Initial**	**1st month**	**2nd month**	**3rd month**	**6th month**
Appearance*	Complies	Complies	Complies	Complies	Complies
Dissolution					
0.5 hrs.	10.16±0.014142	10.15±0.0123	10.11±1.217	10.04±1.028	9.24±1.014
01	24.785±0.841457	23.452±0.157	21.357±0.248	20.425±1.450	20.254±1.514
02	34.92±0.777817	33.751±0.254	32.148±0.175	31.125±0.73	31.324±0.152
04	55.115±0.502046	54.372±0.129	53.142±0.257	54.128±0.172	55.278±1.502
06	64.780±0.692965	63.472±0.257	62.345±0.257	67.710±0.121	66.165±0.203
08	74.735±0.629325	73.176±0.183	72.146±0.135	72.471±0.551	72.147±0.941

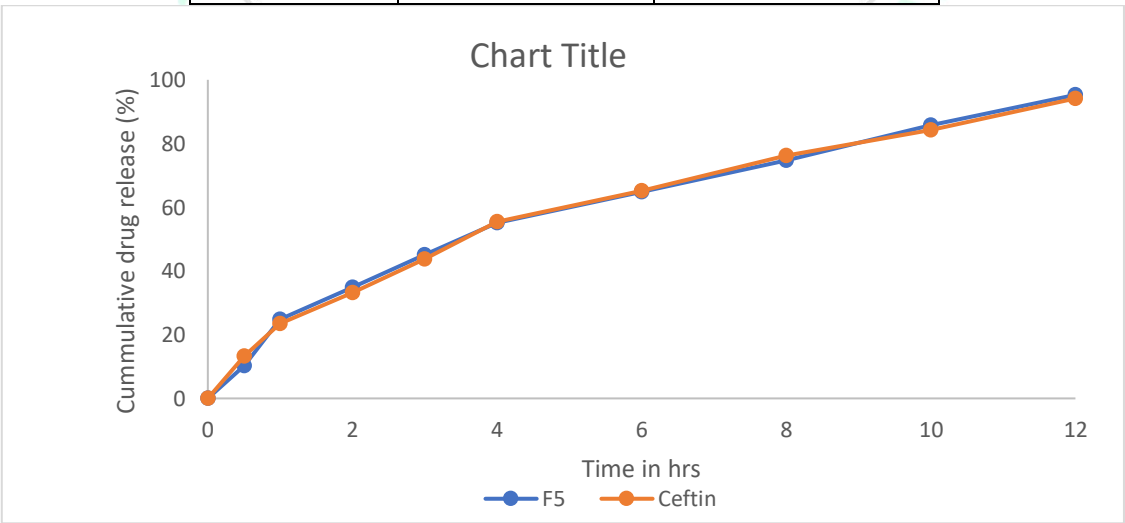
10	85.715±0.643467	84.485±0.184	83.421±0.258	84.177±0.018	83.285±0.756
12	95.27±1.414214	94.27±0.741	93.28±0.157	94.14±0.142	93.458±0.274
Assay (%)	99.47±0.154	98.14±0.154	97.18±0.257	96.25±0.116	95.28±1.458
Friability (%)	0.52±0.052	0.51±0.028	0.50±0.028	0.51±0.017	0.50±0.049
Floating lag time (Sec)	21.49±1.75	21.37±0.29	20.48±0.29	19.76±1.28	18.85±0.207
Swelling Index (Sec)	3.21±0.024	3.20±0.023	3.19±0.047	3.18±0.041	3.17±0.049

Table Comparison of various properties of Optimized formulation F5 and marketed Product

Characteristic Property	Marketed Product	Optimized formulation (F5) (300mg)
Appearance	white to off white in oval shape	white to off whitein oval shape
Length	14.11mm	14.27 mm
Width	4.70 mm	4.95 mm
Thickness	4.50±0.074	4.19±0.084
Hardness	5.11±0.582	5.10±0.421
Average Weight	301.5±0.214	300.4±1.21
Friability	0.55±0.041	0.52±0.052
Dissolution	94.14±1.4417	95.27±1.4142
Assay	98.27±0.253	99.47±0.154

Table Dissolution profile comparison of F5 and Marketed Product

Time (hrs.)	F5 (300mg)	Marketed Product
0.5	10.16±0.014142	13.23±0.024170
1	24.785±0.841457	23.483±0.730034
2	34.92±0.777817	33.189±0.664172
4	55.115±0.502046	55.374±0.401852
6	64.780±0.692965	65.185±0.574120
8	74.735±0.629325	76.238±0.241534
10	85.715±0.643467	84.271±0.152324
12	95.27±1.414214	94.146±0.185416



Comparison dissolution profile of optimised formulation (F5)vsMarketed

Table: Release kinetic data comparison of F5 and Marketed Formulation

Formulation	Zero order	First order	Higuchi plot	Korsemeyer-Peppas plot		Type of drug release mechanism
				R	n	
F5	0.932	0.9466	0.9933	0.5767	0.696	Non fickian transport mechanism
Marketed Product	0.968	0.9341	0.9814	0.6142	0.681	Non fickian transport mechanism

Table Dissolution Profile Comparison Using Similarity Factor (f2)

Time (hrs)	Rt	Tt	{Rt-Tt}	$\{Rt-Tt\}^2$
1	24.65	14.35	10.3	106.09
2	47.64	23.1	24.54	602.211
4	61.76	39.35	22.41	502.208
6	82.74	54.28	28.46	809.971
8	99.18	68.04	31.14	969.69

Conclusion

Floating tablets of Flupirtine increase the GI residence time, as the drug has very little gastric residence time. The floating tablets were obtained and evaluated for pre and post-compression parameters and all the scores were found to be within the range. In Nine formulations, based on a 12-
hour dissolution study F5 is optimized.

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