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DEVELOPMENT AND EVALUATION OF GASTRO RETENTIVE FLOATING DRUG DELIVERY SYSTEM FOR ROPINIROLE HYDROCHLORIDE

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Abstract: Gastro retentive drug delivery systems are some of the best technologies delivered through oral route. These mainly came under study for their effective local action in the GI region, specifically for the drugs with narrow absorption window. Drugs having absorption window in the stomach or upper small intestine have restricted bioavailability and patient compliance's with conventional dosage forms. The gastric residence time of these dosage forms is usually short and they do not show drug release for prolonged period of time. In the recent years, several technologies have evolved showing different mechanisms for retaining the drug in GI region for longer duration with increased bioavailability. Floatable, Mucoadhesive, Swellable, Nano fibrous, High-density and Expandable systems have been explored extensively as the potential gastro-retentive strategies. Interest in gastro retentive drug delivery systems can be attributed to the desire for increased patient convenience.

Key Words – Gastroretentive, Floatable, Mucoadhesive, Swellable, Nano fibrous, Expandable.

INTRODUCTION

The oral route is undertaken as the most advisable route of drug delivery. Effective oral drug delivery may depend upon the several factors like, gastric emptying, gastrointestinal transit time, drug release from the dosage form and site of absorption.[13,35] Most of the oral dosage forms composed of several physiological limitations such as variable gastrointestinal transit and because of variable gastric emptying it leads to non-uniform absorption profiles, incomplete release of drug and very shorter residence time of the dosage form in the stomach. This leads to the lesser absorption of drugs having low absorption window especially in the upper small intestine, as once the drug passes down the absorption site, the remaining quantity of the drug goes unabsorbed.[7,14] The gastric emptying of the drugs in humans is get affected by several factors because of which wide inter and intra subject changes are observed.[2]

In these years, numerous technological improvements have been achieved in the area of controlled release solid oral dosage forms, especially for products, which includes an extended time of release of the drug is sync with an extended gastric retention time.[35] These Gastro Retentive systems have been quite studied because they may improve the in-vivo behavior of many drugs. Gastro retentive drug delivery systems are designed to be retained in the stomach for a prolong time and release there active ingredient and thereby enable sustained and prolonged input of the drug to the upper part of gastrointestinal tract.[15,36] Some drugs have their greatest therapeutic effect when released in stomach with lesser side effect particularly when the released is prolonged in continuous and control manner. This system provide there therapeutic effect without the need of repeated dosages or with low dosage frequency. Since many drugs are absorbed up to the level in the upper part of the gastrointestinal tract, this high variability can lead to non-uniform absorption and makes the bioavailability unpredictable.[13,41]

All these requirements can make it effective delivery of the drugs to the absorption windows, for local action and for the treatment of gastric disorders such as gastro-oesophageal reflux, may be achieved due to floating drug delivery systems.[37] Till now, a number of Floating DDS containing various technologies, carrying their own pros and cons were developed such as, hydro dynamically balanced systems, gas generating systems, hollow microspheres and lastly raft forming systems, high density sinking systems that is retained in the bottom of the stomach, low density floating systems that makes buoyancy in

gastric fluid, mucoadhesive systems that due bio adhesion to the stomach mucosa, unfordable, extendible, or swellable systems which control emptying of the dosage forms passing by the pyloric sphincter of the stomach, porous hydrogel systems, magnetic systems etc.[39] The hydrodynamic balanced system also called Floating drug delivery system (FDDS) is an oral dosage form designed to prolong the residence time of the dosage form within the GIT. It consists of the formulation of a drug with gel forming hydrocolloids which are meant to remain buoyant in the stomach fluids. Drug dissolution and the release of drug from the dosage form retained in the stomach fluids occur at the various pH of the stomach under controlled conditions.[35] However, the system may be used for most of the drugs where time dependent release of the drug is functioned by the oral route. The formulation of these dosage forms should comply with mentioned major criteria for HBS.

1. It must have ability to form a cohesive gel barrier.
2. It should maintain an overall specific gravity less than that of gastric content.
3. It should dissolve slowly enough to serve as a "Reservoir" for the delivery system.

MATERIALS

Ropinirole hydrochloride was obtained as a gift sample from Alembic Pharmaceuticals Ltd., Vadodara. HPMC K4M was obtained as a gift sample from Colorcon, Goa. Sodium Alginate were procured from S. D. Fine chemicals, Mumbai, India. All other chemicals and excipients used were of analytical grade commercially obtained from S. D. Fine chemicals, Mumbai, India.

METHOD

Selection of Active Pharmaceutical Agent

Ropinirole Hydrochloride is the hydrochloride salt form of Ropinirole, which is a non-ergot dopamine agonist possessing antiparkinsonian property. It acts as a substitute for dopamine and binds and activates Dopamine D2 and D3 receptors within the caudate putamen in the brain, thereby improving motor function.

Preparation of Gastro Retentive Floating Tablet.

Unit operations for tablet preparation by direct compression method. The amount of API (Ropinirole Hydrochloride) and excipients required for batch of tablet formulation were weighed using electronic weighing balance. After weighing of all the API and excipients, they were pass through sieve no. 40 to break agglomerates if any present in the raw materials for its uniform distribution. Then all polymer and excipients except magnesium stearate and talc were mixed manually by using mortar pestle. And the prepared blend was lubricated using magnesium stearate and talc in mortar pestle for 15 minutes. Finally the prepared blend was compressed using standard 10 mm round, flat punch.

Name of Ingredients	**Quantity Taken (mg)**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Ropinirole HCl	01	01	01	01	01	01	01	01	01
Sodium Alginate	**25**	**25**	**25**	**50**	**50**	**50**	**75**	**75**	**75**
HPMC K4M	**25**	**50**	**75**	**25**	**50**	**75**	**25**	**50**	**75**
Sod. Bicarbonate	60	60	60	60	60	60	60	60	60
Citric Acid	30	30	30	30	30	30	30	30	30
MCC	102	77	52	77	52	27	52	27	02
Talc	04	04	04	04	04	04	04	04	04
Magnesium Stearate	02	02	02	02	02	02	02	02	02
Aerosile	01	01	01	01	01	01	01	01	01
Total	250	250	250	250	250	250	250	250	250

EVALUATION OF GASTRO RETENTIVE FLOATING TABLET

DRUG AND POLYMER COMPATIBILITY STUDIES - The FTIR spectrum of drug was recorded on an infrared spectrophotometer (Shimadzu Affinity-1). IR spectrum the of drug, polymers, and their physical mixture were recorded in the frequency range of 400-4000 cm-1. The recorded peaks were then noted and matched with standard FTIR of the drug.

CALIBRATION CURVE OF ROPINIROLE HCL IN 0.1N HCL - From solution having concentration 100 µg/ml aliquots of 0.2, 0.4, 0.6, 0.8, 1.0, 1.2,1.4, 1.6, 1.8, and 2 ml were pipette out into 10 ml volumetric flasks. The volume was made up to the mark with 0.1N HCL to get the final concentration of 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20 µg/ml respectively. The absorbance of each concentration was measured at 250 nm. A graph of absorbance versus concentration was plotted. It shows the straight line which means calibration curve obeys the Beers Lamberts law.

PRECOMPRESSION STUDY

Angle of Repose - The angle of repose is the maximum angle that the plane of powder makes with the horizontal surface on rotation. Angle of repose is helpful in assessment of flow properties of particles which could be further related to packing densities and mechanical arrangements of particles. The angle of repose of powder was determined by the fixing the funnel and free standing cone method. The precisely weighed granules were taken. The height of the funnel was then adjusted in such a manner, the tip of the funnel should just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surfaces. The diameter of the powder cone measured and angle of repose was calculated.

Determination of Bulk density – Apparent bulk density can be determined by pouring preserved bulk powder into a graduated measuring cylinder via a large funnel and measuring the volume and weight of the powder. Bulk density can be calculated by the following formula,

$$\text{Bulk Density} = \frac{\text{Weight}}{\text{Bulk Volume (Vo)}}$$

Where,
V_o – Bulk Volume

Determination of Tapped density - Tapped density can be determined by pouring preserved powder into a graduated measuring cylinder via a large funnel and tapped for 100 times on a wooden plank and measuring the volume and weight of the powder. Tapped density can be calculated by the following formula

$$\text{Tapped Density} = \frac{\text{Weight}}{\text{Tapped Volume (Vt)}}$$

Where,
V_t – Tapped Volume

Compressibility Index (or) Carr' index (I) – An indirect method of measuring powder flow from bulk densities was developed by Carr. The percentages of compressibility of the powder is a direct measure of the potential powder arch and stability. Carr's index of the each formulation prepared was calculated.

Hausner's ratio – Hausner's ratio indicates the flow properties of the powder and is measured by the ratio between tapped density and bulk density. Hausner's found that this ratio was related to inter particle friction and, as such, could be used to predict powder flow properties

POST COMPRESSION STUDY

Dimensions – Control of physical dimension of the tablets such as thickness and is essentials for consumer acceptance and tablets uniformity. The thickness and diameter of the tablets are carried out using digital Vernier Calliper. Three tablets are used from each batch and the results are expressed in Millimetre (mm).

Weight Variation Test – Twenty tablets are selected at random, individually weighed in a single pan electronic balance and the average weight is calculated. As per IP not more than two of individual weights should deviate from average weight by more than 5% and none deviate more than twice that Percentage.

Hardness Test –The tablet was held between a fixed and moving jaw. Scale was adjusted to zero and then load is gradually increase till the tablet starts to break. The value of the load at that point gives the hardness of the tablet. Three tablets from each batch are used for hardness test and results are expressed in Kg/cm^2.

Friability Test – Pre weighed samples of 20 tablets are placed in the friabilator, which is then operated for 100 revolutions (4 min). The tablets are then dusted and reweighed. Compressed tablets that loss less than 0.5 to 1.0% of their weight are generally considered acceptable.

***In vitro* Floating Study -** The floating capacity of the tablets was determined using USP Dissolution apparatus II containing 900 ml of simulated gastric fluid. The time interval between introduction of the tablet in to the dissolution medium and its buoyancy to the dissolution medium was taken as buoyancy Lag Time and for which time the tablet constantly floats on the surface of the medium was taken as Total Floating Time.

Determination of Drug Content - Ten tablets are weighed and taken in a mortar and crushed to make powder form. A quantity of powder weighing equivalent to 10 mg of drug is taken in a 100 ml volumetric flask and 0.1 N HCl was added. The solution is filtered using membrane filter (0.45µm) and 10 ml of filtrate is taken into 100 ml volumetric flask and made up to final volume with 0.1 N HCl. Then its absorbance is measured at 250 nm using UV Visible spectrometer. Then the amount of total drug present in the one tablet is calculated.

***IN - VITRO* DRUG RELEASE STUDIES**

Dissolution characteristics of the formulated floating tablets of Ropinirole hydrochloride was carried out using USP Type II (paddle) dissolution test apparatus for 8 hrs.

Method - 900 ml of 0.1 N HCl was filled in dissolution vessel and temperature of the medium is set at 37°C ± 0.5°C. One tablet of different batch is placed in each dissolution vessel and the rotational speed of paddle was set at 50 rpm. 5ml of sample is withdrawn at pre-determined time interval of every one hour for up to 8 hours and same volume of fresh medium is replaced immediately. The withdrawn sample is diluted to 10 ml in volumetric flask and filtered through 0.45µ membrane filter. The resultant samples are analysed for drug content at 250 nm using UV-Visible spectrophotometer.

DETERMINATION OF SWELLING INDEX

For each formulation batch, one tablet was weighed and placed in a beaker containing 200 ml of media. After each interval, the tablet should be removed from the media and weighed again up to 24 hours and note down the readings.

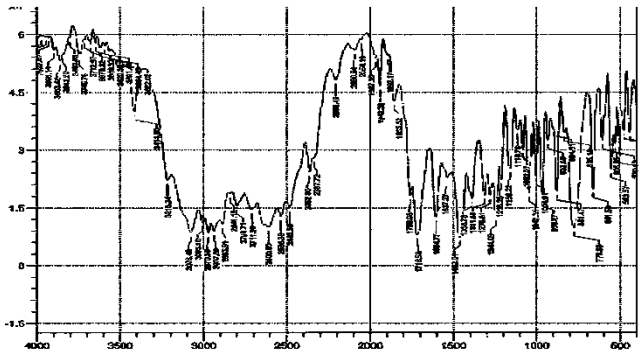
STABILITY STUDIES

In the present study, stability studies were carried out at 40°C ± 2°C, 75 ± 5% RH), (25°C ± 2°C ,75% ± 5% RH) and (40°C ± 2°C, 75% ± 5% RH) for a specific time period up to 1 month for the optimized formulation. The optimized formulation was analysed for the drug contents study, pH, lag time (sec), floating time (hours), cumulative drug release (%). Experiments were performed in triplicate and average values are noted. The stability studies data was then recorded.

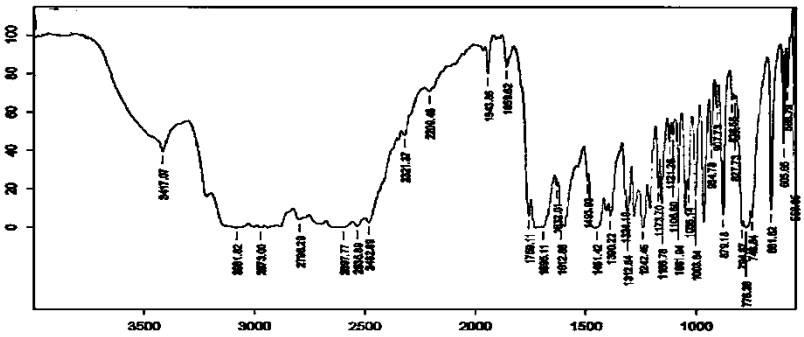
RESULTS AND DISCUSSION

EVALUATION OF GASTRO RETENTIVE FLOATING TABLET

Drug and polymer compatibility studies –



A.



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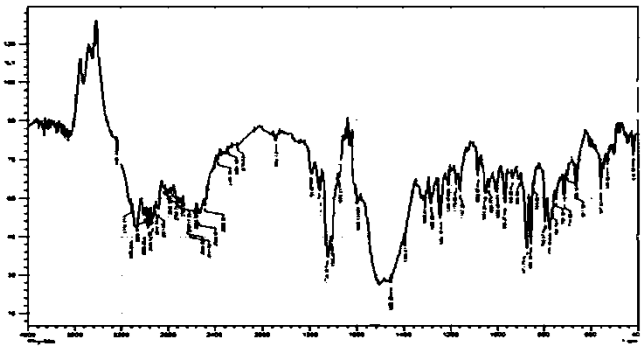


C.

Graph no. 1 – FTIR of Ropinirole Hydrochloride and physical mixtures with polymers

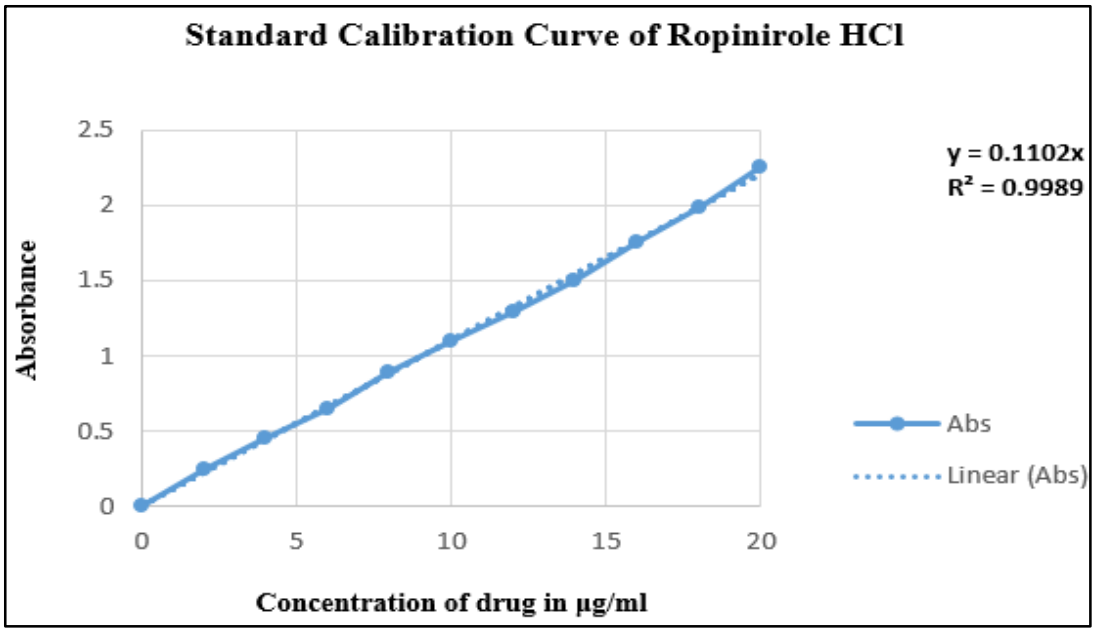
A – FTIR of Ropinirole Hydrochloride

B – FTIR of Ropinirole Hydrochloride + Sodium Alginate

C – FTIR of Ropinirole Hydrochloride + HHPMC K4M

The results of FTIR study shows that, the drug was not found to show any interactions with the polymers i.e. sodium alginate and HPMC K4M. Hence we can use the chosen polymers for further study.

Calibration Curve of Ropinirole HCl In 0.1N HCl –



Graph no. 2 – Calibration curve of Ropinirole Hydrochloride in 0.1 N HCl

The calibration curve of Ropinirole HCl shows the R^2 value which is equals to 0.9989 nearly a straight line which shows that the study follows beers law.

PRECOMPRESSION STUDY

Table no. 1 – Pre – compression study of factorial batch

Batch	Bulk Density (g/cm^3 ± SD)	True Density (g/cm^3 ± SD)	Carr's Index (% ± SD)	Hausners Ratio (± SD)	Angle of Repose (θ ± SD)
F1	0.461 ± 0.002	0.527 ± 0.009	12.52 ± 0.78	1.14 ± 0.05	31.23 ± 1.15
F2	0.459 ± 0.008	0.523 ± 0.015	12.24 ± 0.96	1.14 ± 0.04	32.40 ± 1.09
F3	0.464 ± 0.005	0.542 ± 0.019	14.39 ± 0.71	1.16 ± 0.05	32.57 ± 1.44
F4	0.448 ± 0.012	0.511 ± 0.021	12.32 ± 0.75	1.14 ± 0.03	31.41 ± 1.18
F5	0.451 ± 0.006	0.519 ± 0.007	13.10 ± 0.68	1.15 ± 0.02	31.56 ± 1.23
F6	0.438 ± 0.011	0.508 ± 0.023	13.77 ± 0.56	1.16 ± 0.05	32.15 ± 1.41
F7	0.443 ± 0.009	0.514 ± 0.008	13.81 ± 0.44	1.16 ± 0.07	31.58 ± 1.34
F8	0.458 ± 0.013	0.525 ± 0.014	12.76 ± 0.90	1.14 ± 0.09	33.05 ± 1.04
F9	0.469 ± 0.005	0.534 ± 0.009	12.17 ± 0.84	1.13 ± 0.08	32.45 ± 1.19

n = 3

POST COMPRESSION STUDY

Table no. 2 – Post – compression study of factorial batch combinations.

Batch	Wt. variation (± SD)	Hardness (± SD)	Diameter (± SD)	Thickness (± SD)	Friability (± SD)	FLT (± SD)	TFT (± SD)	Drug Content
F1	249.96±0.598	5±0.051	9.013±0.156	2.733±0.013	0.36±0.0025	88±0.669	12±0.11	98.9±0.84
F2	249.81±0.601	4.6±0.059	9.014±0.156	2.751±0.015	0.40±0.0018	95±0.661	12±0.09	96.8±0.89
F3	249.72±0.554	4.6±0.058	9.014±0.156	2.745±0.018	0.52±0.0019	106±0.559	12±0.13	97.09±0.11
F4	249.76±0.578	5±0.054	9.014±0.156	2.749±0.009	0.36±0.0025	108±0.631	12±0.12	96.18±0.96
F5	249.87±0.503	5±0.055	9.013±0.156	2.744±0.011	0.38±0.0021	113±0.651	12±0.11	98.91±0.95
F6	250.56±0.616	4.8±0.059	9.014±0.156	2.739±0.008	0.41±0.0025	109±0.421	12±0.15	97.09±0.87
F7	249.78±0.548	5±0.057	9.014±0.156	2.748±0.017	0.41±0.0018	92±0.605	12±0.08	96.18±0.91
F8	249.43±0.532	4.8±0.055	9.013±0.156	2.752±0.015	0.39±0.0017	188±0.631	12±0.13	97.09±0.95
F9	250.12±0.628	5.16±0.05	9.013±0.156	2.748±0.019	0.42±0.009	205±0.643	12±0.11	99.81±0.97

n = 3

The **Average Weight** of all floating tablets within formulation was found to be uniform. This indicates uniform filling of the die cavity during tablet compression.

The **Hardness** of all floating tablets was found to be in the range of 4.6±0.059 to 5.16±0.05 kg/cm2. This insures good mechanical strength.

The **Thickness** of all floating tablets was found in the range of 2.733±0.013 to 2.752±0.015 mm. There were no marked variations in the thickness of all formulation indicating uniform behaviour of powder throughout the compression process.

The **Friability** of all floating tablets was found to be in range 0.36±0.0025 to 0.52±0.0019,which indicates the good flow ability.

The **Drug Content** of all formulations was found to be in between 96.8±0.89 to 99.81±0.97 %. The values ensures good uniformity of drug content in the tablet.

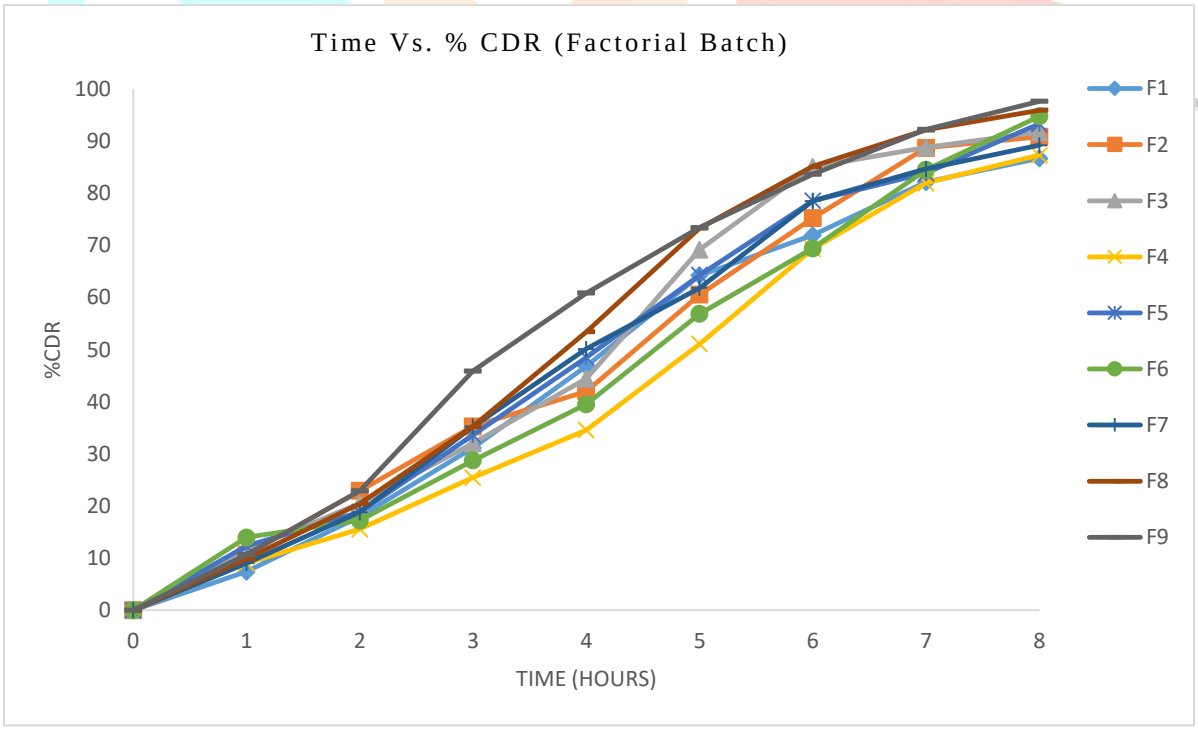
From the results it was observed that, **Floating Lag Time (FLT)** of all formulations was in range 88±0.669 to 205±0.643 seconds.

IN - VITRO DRUG RELEASE STUDIES

Table no. 3 – In vitro drug release study of factorial batch.

Time (Hrs)	% Cumulative Drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
1	7.391 ± 0.198	10.676 ± 0.169	11.497± 0.165	9.033 ± 0.191	12.318 ± 0.175	13.96 ± 0.198	9.033 ± 0.195	9.854 ± 0.191	10.676 ± 0.188
2	18.008 ± 0.185	22.926 ± 0.199	20.481 ± 0.178	15.567 ± 0.184	18.852 ± 0.188	17.227 ± 0.191	18.833 ± 0.197	20.471 ± 0.195	22.92 ± 0.165
3	31.175 ± 0.191	35.303 ± 0.181	32.028 ± 0.191	25.453 ± 0.175	33.656 ± 0.176	28.756 ± 0.195	35.272 ± 0.181	35.285 ± 0.197	45.921 ± 0.176
4	46.864 ± 0.198	42.032 ± 0.187	44.455 ± 0.195	34.578 ± 0.189	48.543 ± 0.198	39.532 ± 0.178	50.167 ± 0.179	53.448 ± 0.181	60.875 ± 0.188
5	64.274 ± 0.198	60.562 ± 0.195	69.201 ± 0.178	51.102 ± 0.175	64.328 ± 0.191	56.901 ± 0.185	61.878 ± 0.156	73.343 ± 0.176	73.461 ± 0.185
6	71.978 ± 0.179	75.263 ± 0.173	85.099 ± 0.199	69.351 ± 0.165	78.566 ± 0.195	69.464 ± 0.198	78.552 ± 0.186	85.181± 0.165	83.666 ± 0.196
7	82.173 ± 0.177	88.743 ± 0.189	88.833 ± 0.181	81.982 ± 0.159	83.897 ± 0.165	84.546 ± 0.169	84.711 ± 0.169	92.182 ± 0.178	92.291 ± 0.185
8	86.705 ± 0.165	90.862 ± 0.189	91.769 ± 0.177	87.332 ± 0.169	93.339 ± 0.178	94.809 ± 0.191	89.246 ± 0.188	95.952 ± 0.195	97.695 ± 0.177

n = 3



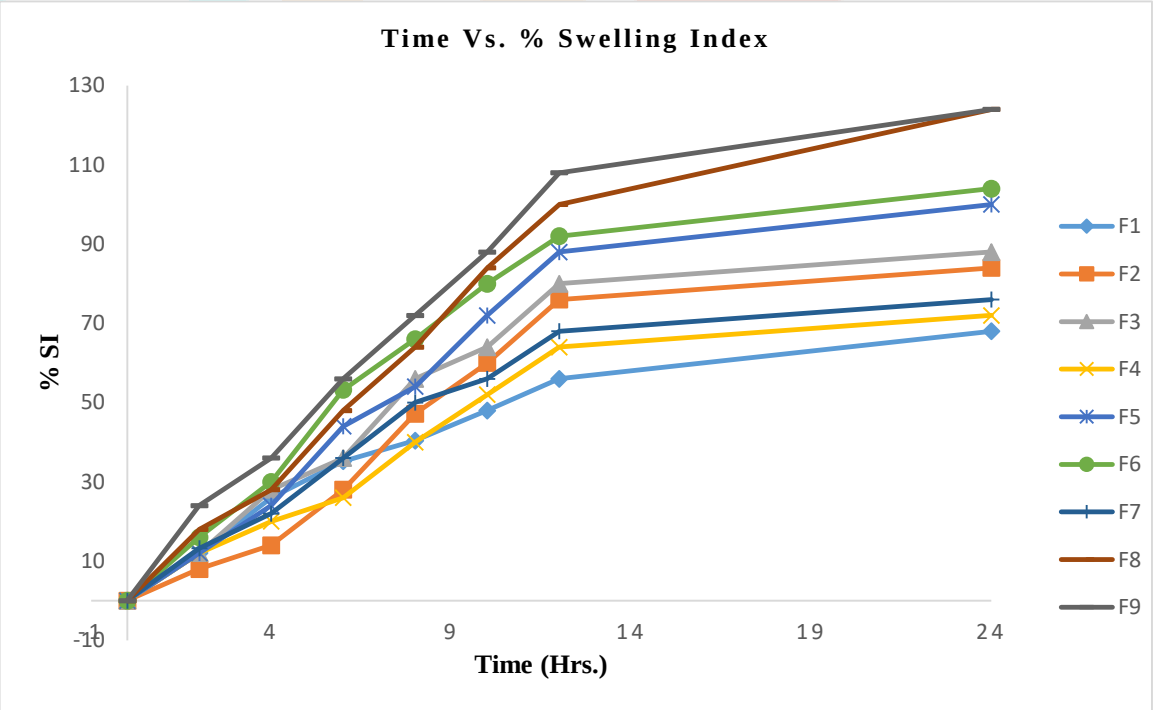
Graph no. 3 – Time vs. % CDR (Factorial Batch)

DETERMINATION OF SWELLING INDEX

Table no. 4 – % Swelling Index of Factorial Batch

n = 3

Time (Hrs)	F1 ± SD	F2 ± SD	F3 ± SD	F4 ± SD	F5± SD	F6 ± SD	F7 ± SD	F8 ± SD	F9 ± SD
0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
2	12 ± 0.895	8 ± 0.895	12 ± 0.895	12 ± 0.895	12 ± 0.895	16 ± 0.895	13.2 ± 0.895	18 ± 0.895	24 ± 0.895
4	26 ± 0.605	14 ± 0.895	28 ± 0.895	20 ± 0.895	24 ± 0.895	30 ± 0.895	22 ± 0.895	28 ± 0.895	36 ± 0.895
6	35.2 ± 0.712	28 ± 0.895	36 ± 0.895	26 ± 0.895	44 ± 0.895	53.2 ± 0.895	36 ± 0.895	48 ± 0.895	56 ± 0.895
8	40.4 ± 0.887	47.2 ± 0.895	56 ± 0.895	40 ± 0.895	54 ± 0.895	66 ± 0.895	50 ± 0.895	64 ± 0.895	72 ± 0.895
10	48 ± 0.568	60 ± 0.895	64 ± 0.895	52 ± 0.895	72 ± 0.895	80 ± 0.895	56 ± 0.895	84 ± 0.895	88 ± 0.895
12	56 ± 0.897	76 ± 0.895	80 ± 0.895	64 ± 0.895	88 ± 0.895	92 ± 0.895	68 ± 0.895	100 ± 0.895	108 ± 0.895
24	68 ± 0.689	84 ± 0.895	88 ± 0.895	72 ± 0.895	100 ± 0.895	104 ± 0.895	76 ± 0.895	124 ± 0.895	124 ± 0.895



Graph no. 4 – Time vs. % Swelling Index

STABILITY STUDIES

Table no. 5 – Stability study at 40°C ± 2°C / 75 ± 5% RH

Time	% Drug Content	Lag Time (Sec)	Floating Time (Hrs)	%CDR	
				After 12 Hrs.	After 24 Hrs.
0 Days	99.15 ± 0.03	94 ± 0.643	12 ± 0.245	75.02 ± 0.484	87.28 ± 586
1 Weeks	99.18 ± 0.03	94 ± 0.643	12 ± 0.251	75.02 ± 0.413	87.28 ± 555
2 Weeks	99.15 ± 0.03	94 ± 0.643	12 ± 0.219	75.02 ± 0.456	87.28 ± 562
3 Weeks	99.15 ± 0.03	94 ± 0.643	12 ± 0.233	75.02 ± 0.478	87.28 ± 581
4 Weeks	99.14 ± 0.03	94 ± 0.643	12 ± 0.242	75.02 ± 0.468	87.28 ± 509

n = 3

Table no. 6 – Stability study at 25°C ± 2°C / 75 ± 5% RH

Time	% Drug Content	Lag Time (Sec)	Floating Time (Hrs)	%CDR	
				After 12 Hrs.	After 24 Hrs.
0 Days	99.15 ± 0.03	94 ± 0.643	12 ± 0.255	75.02 ± 0.484	87.28 ± 586
1 Weeks	99.18 ± 0.03	94 ± 0.643	12 ± 0.269	75.02 ± 0.413	87.28 ± 555
2 Weeks	99.15 ± 0.03	94 ± 0.643	12 ± 0.238	75.02 ± 0.456	87.28 ± 562
3 Weeks	99.15 ± 0.03	94 ± 0.643	12 ± 0.231	75.02 ± 0.478	87.28 ± 581
4 Weeks	99.14 ± 0.03	94 ± 0.643	12 ± 0.248	75.02 ± 0.468	87.28 ± 509

n = 3

Table no. 7 – Stability study at 10°C ± 2°C / 75 ± 5% RH

Time	% Drug Content	Lag Time (Sec)	Floating Time (Hrs)	%CDR	
				After 12 Hrs.	After 24 Hrs.
0 Days	99.15 ± 0.03	94 ± 0.643	12 ± 0.271	75.02 ± 0.476	87.28 ± 586
1 Weeks	99.18 ± 0.03	94 ± 0.643	12 ± 0.238	75.02 ± 0.425	87.28 ± 555
2 Weeks	99.15 ± 0.03	94 ± 0.643	12 ± 0.202	75.02 ± 0.475	87.28 ± 562
3 Weeks	99.15 ± 0.03	94 ± 0.643	12 ± 0.231	75.02 ± 0.478	87.28 ± 581
4 Weeks	99.14 ± 0.03	94 ± 0.643	12 ± 0.254	75.02 ± 0.468	87.28 ± 509

n = 3

The performed stability studies of optimum formulation F9 revealed that there is very slight reduction in drug content was observed over the period of 4 weeks. No significant changes was observed on % cumulative drug release (after 24 hours), lag time and total floating time at various storage conditions i.e. (**40°C ± 2°C / 75 ± 5% RH), (25°C ± 2°C / 75 ± 5% RH)** and (**25°C ± 2°C / 75 ± 5% RH).** Hence, the optimised formulation F9 was found to be stable for the duration of one month.

CONCLUSION

A 3^2 factorial design was performed to study the effect of formulation variables on FLT, drug content and *in vitro* drug release. Further the release from the floating studies suggested that the desired floating profile of gastroretentive floating drug delivery system could be achieved while maintaining the desired release properties of formulation. The statistical approach for formulation optimization is useful tool, particularly when two or more variables are to be evaluated simultaneously. The variables HPMC K4M and sodium alginate evaluated in this study exhibited significant effect on the responses FLT and % CDR of the formulations; however the HPMC K4M markly affected the release profile.

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