CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.7988711

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

FORMULATION AND EVALUATION OF GASTRO RETENTIVE FLOATING TABLET USING RIVASTIGMINE TARTRATE

Hemangi P. Vaishnav*, Nisahn N. Bobade, Shrikant D. Pande

Vidyabharati college of pharmacy, C. K. Naidu Road, Camp, Amravati, Maharashtra, India –444602.

Abstract:

The present investigation was a successful attempt to develop gastro retentive floating tablet of Rivastigmine Tartrate in order to improve controlled release of drug. The formulation was effectively prepared using biocompatible polymer HPMC K4M and sodium alginate chosen in appropriate concentration with the drug. The gastro retentive floating tablet was preapared by direct compression method by applying 3^2 factorial designs. HPMC K4M (X1) and Sodium Alginate (X2) were selected as independent variables, and nine formulations were prepared in accordance with the experimental design. The prepared tablet was evaluated for different parameter such as wight variation, hardness, friability, floating time, drug content, in vitro dissoluation, swelling index and Dissolution data were analyse for kinetic model to study kinetic release of drug. From the evaluation of floating tablet of rivastigmine tartrate, F6 batch shown results were within limits and % CDR (98.559 ± 0.197) and buoyant up to 12 hours. Therefor, batch F6 was concluded as optimized formulation that could release drug in stomach at controlled release manner and prove to be potential candidate for safe and effective formulation for prolonged period of time.

Keywords: Rivastigmine tartrate, floating tablet, gastro-retentive, 3^2 factorial designs, Anti'alzheimer, dementia.

Corresponding author:

Hemangi P. Vaishnav,

Vidyabharati college of pharmacy,
C. K. Naidu Road, Camp, Amravati,
Maharashtra, India –444602.

hemangivaishnav181@gmail.com

QR code

Please cite this article in press Hemangi P. Vaishnav et al, ***Formulation And Evaluation Of Gastro Retentive Floating Tablet Using Rivastigmine Tartrate****., Indo Am. J. P. Sci, 2023; 10 (05).*

INTRODUCTION:

The oral route is among the most and appropriate route for many medications. The oral route is increasingly being used for delivery of therapeutic agents to systemic circulation because the low cost of the therapy and ease of administration lead to high level of patient compliance [1]. A controlled release drug delivery system can maintain the ideal therapeutic drug concentration in the blood at a predictable and reproducible release rate over a prolonged period of time, enhancement of activity of duration for short half-life drugs, elimination of side effects, reducing frequency of dosing, optimized therapy and better patient compliance [2]. The bulk density of the floating drug delivery system is lower than that of gastric fluid, so it remained prolonged in the stomach or other targeted site and distributes the drug in a controlled manner. Over a longer period of time, the floating medication administration has no influence on the rate of stomach emptying [3].

Rivastigmine Tartrate is reversible cholinesterase inhibitor. It is used to treat mild to moderate dementia caused by Alzheimer or Parkinson disease. Rivastigmine tartrate shows bioavaibility approximately 36%, and biological half-life is 1.5 hour, metabolise by hepatically. Which make it a suitable candidate for gastro-retentive floating controlled release action of drug from the formulation[4]. In present study gastro retentive Floating Tablet were prepared of Rivastigmine Tartrate are formulated to prolong the residence time at the absorption site to facilitate intimate contact with the absorption surface and thereby improve and enhance the bioavaibility.

MATERIAL AND METHOD:

Material:

Rivastigmine Tartrate was procured as a gift sample from "Sun pharma, Vadodara". HPMC K4M obtained as a gift sample from colorcon Asia pvt ltd., goa. Sodium Alginate obtained from Loba chemicals Pvt. Ltd. Mumbai, Citric Acid, Sodium Bicarbonate, MCC, Magnesium Sterate, And Aerosile 200 was procured from S.D. Fine Chemicals ltd, Mumbai.

Method:

Selection of drug

Rivastigmine Tartrate was selected for present study. It has short biological half- life of about 1.5 hours and low bioavaibility (36%). The floating Tablet of Rivastigmine Tartrate would prolong the residence time at the absorption site to facilitate intimate contact with the absorption surface and thereby improve and enhance the bioavaibility.

Preparation Of Gastro retentive Floating Tablet [6]

A factorial batch is used to evaluate two or more factor simultaneously. The treatment is combination of level of factors. The advantages of factorial designs over one factor at-a-time experiments include their efficiency and deletion of interaction. Intervention studies with two or more categorical explanatory variable leading to numerical outcome variable are called factorial designs. A factor is simply a categorical variable with two or more value refers as levels. A study in which there are two factors with theirs three levels called 3^2 factorial designs. A for the present work 3^2 factorial was selected. The two independent variables were selected HPMC K4M and Sodium Alginate and nine formulations prepared as per experimental design.

Table 1: Amount Of Variable In 3^2 Factorial Designs Batches.

Coded value	Actual value	
	X1 HPMC K4M	X2 Sodium Alginate
-1	50mg	50mg
0	75mg	75mg
+1	100mg	100mg

Gastro retentive floating tablets were prepared by employing direct compression method as per formula mentioned in Table No 2. API and polymers i.e., HPMC K4M and Sodium Alginate, base i.e. sodium bicarbonate, acidifying agent i.e. citric acid and glidants i.e. talc were screened through sieve no. 60. All ingredients were weighed in precise manner. Then the ingredients were subjected to mixing for a period of 10 minutes. In the final stage, lubricants i.e., magnesium stearate and aerosil was added in the mixture and mixed for further 5 minutes. Finally, the powder is punched into using the rotary tablet punching machine using flat bevelled punch.

Table No. 2 - Formula for gastro retentive floating tablet of Rivastigmine Tartrate

Name of Ingredient	**Quantity taken (mg)**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Rivastigmine tartrate	10	10	10	10	10	10	10	10	10
HPMC K4M	**50**	**50**	**50**	**75**	**75**	**75**	**100**	**100**	**100**
Sodium alginate	**50**	**75**	**100**	**50**	**75**	**100**	**50**	**75**	**100**
Citric acid	30	30	30	30	30	30	30	30	30
Sodium bicarbonate	60	60	60	60	60	60	60	60	60
MCC	118	68	18	93	68	93	43	68	43
Talc	4	4	4	4	4	4	4	4	4
Magnesium stearate	2	2	2	2	2	2	2	2	2
Aerosile	1	1	1	1	1	1	1	1	1

Evaluation parameters of floating tablet

Drug And Polymer Compatibility Studies [7]

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 observed peaks were then recorded and contrasted to the drug's standard FTIR.

Pre - Compression Parameters

1. Angle of Repose [8] **-** The angle of repose is the maximum angle that the plane of powder makes with the horizontal surface. The angle of repose of powder was determined by the fixed funnel and free-standing cone method. The precisely measured powder was placed into a funnel. The funnel's height was adjusted such that the tip of the device just rested the apex of the powdered pile. The powder was allowed to flow through the funnel freely onto the surfaces. The diameter was measured and angle of repose was calculated using the following equation,

$$\tan\theta = \frac{h}{r}$$

Where,
h = Height of the powder heap
r = Radius of the powder heap
θ = Angle of repose.

2. Determination of Bulk Density[9] **–** 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,

$$\text{Bulk Density} = \frac{\text{Weight}}{\text{Bulk volume}}$$

3. Determination of Tapped density[9] – Tapped density can be determined by pouring preserved powder into a graduated measuring cylinder via a large funnel and tapped for 100 times on measuring the powder's weight and volume with a wooden plank. Tapped density can be calculated by the following formula,

$$\text{Tapped Density} = \frac{\text{Weight}}{\text{Tapped Volume}}$$

4. Compressibility Index (or) Carr's Index [10] **–** An indirect method of measuring powder flow from bulk densities was developed by Carr's. The percentages compressibility of a powder was a direct measure of the potential powder arch or bridge strength and stability. Each formulation's Carr's index was estimated using the equation below,

$$\text{Carr's Index (\%)} = \text{Tapped Density} - \text{Bulk Density} \times 100$$

5. Hausner's ratio [11] **–** Hausner's ratio indicates the flow properties of the powder and is measured by the ratio of Tapped density to bulk density. The tapped density to bulk density ratio is what characterises it. Hausner's found that this ratio was related to inter particle friction and, as such, could be used to predict

powder flow properties. Generally a value less than 1.25 indicates good flow properties, which is equivalent to 20% of Carr's index,

$$\text{Hausners Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

Post – Compression Parameters

The gastro retentive floating tablet were assessed for different post compression evaluation such as General appearance, tablet diamention, weight variation test, hardness, friability, drug content test, and in vitro floating duration time. [12, 13]

1. General Appearance – The general appearance of the tablets from each formulation batch was observed. The general parameters are shape, colour, presence or absence of odour were evaluated visually by randomly observing any tablet from formulated batches.

2. Tablet Dimensions – Physical dimension of the tablets such as thickness and diameter are essential for acceptance and tablets uniformity. The measurement of thickness and diameter of the tablets are carried out by using digital thickness tester. Three tablets were used from each batch and then evaluated for their dimensions and results were expressed in millimetre (mm).

3. Weight Variation Test – Twenty tablets are selected at random, individually weighed in electronic balance and the average weight was calculated. The weight uniformity was assessed in accordance with I.P. specifications. An average of two individual weights should differ from the average weight by more than 5 according to IP.

4. Hardness Test – The hardness tester's moving and fixed jaws were used to hold the tablet in place. The strain was steadily increased until the tablets were shattered when the scale was set to zero. The amount of force there provides a measurement of the tablet's hardness. To survive mechanical shocks from handling during manufacture, packing, and shipment, tablets must have a particular level of hardness. For the hardness test, three tablets from each batch are utilised, and the findings are given in kg/cm2.

5. Friability Test – It is carried out in a roche friabilator apparatus, in which the tablets are subjected to the combined action of abrasion and shock by utilising a plastic chamber that revolves at 25 rpm and drops the tablets at a distance of 6 inches on revolution. Pre weighed 10 tablets are placed in the friabilator, which is then operated for 100 revolutions (4 minutes). The tablets are then dusted and reweighed. The percentage friability is calculated by using following equation,

$$\% \text{ Friability} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Final Weight}} \times 100$$

6. Drug Content – Ten tablets are weighed and taken in a mortar and crushed to make powder form. A quantity of powder weighted equivalent to 10 mg of drug is taken in a 100 ml of 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, a UV-visible spectrometer is used to determine its absorbance at 250 nm. The amount of drug present in one tablet is calculated using following equation,

$$\% \text{ Drug Content} = \frac{\text{Absorbance} \times 100}{\text{Weight Taken}}$$

7. In Vitro Floating Duration Time – The floating capacity of the tablets were determined by using USP dissolution apparatus II containing 900 ml of 0.1 N HCl. The time interval between introduction of the tablet into dissolution medium and its buoyancy to dissolution medium was taken as buoyancy lag time. Total floating time was the time taken by the tablet to constantly floats on the surface of the medium, which was observed visually and taken as floating duration.

In vitro drug release study [14]

Using USP type II (paddle) dissolution test apparatus, the dissolution characteristics of the formed floating tablets of rivastigmine tartrate were examined for 12 hours.

Method: 900 ml of 0.1 N HCl was filled in dissolution vessel and temperature of the medium was set at 37°C ± 0.5°C. One tablet of each batch was placed in each dissolution vessel and the rotational speed of paddle was set at 50 rpm. 5 ml of sample is withdrawn at predetermined time of one hour 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 263 nm using UV-Visible spectrophotometer.

Determination of Swelling Index [15, 16]

Excipients in tablets can swell by absorbing fluids, which causes them to gain weight and volume. Liquid uptake by the particle may result via hydration of macromolecules or saturation of capillary spaces

inside the particles. Through pore-like openings, the liquid infiltrates the particles and binds to the big molecules, breaking the hydrogen bond and causing the particle to inflate. The amount of swelling can be expressed in terms of the tablet's percentage weight gain.

Method: One tablet from each formulation batch was weighed and put into a beaker with 200 ml of medium. The tablet was taken out of the beaker and weighed again up to 24 hours later at each interval. The following formula was used to determine the swelling index,

$$\text{Swelling Index} = \frac{Wt - Wo}{Wo}$$

Where,
Wt. = Weight of tablet at time t
Wo = Weight of tablet before placing in the beaker

Kinetics of drug release [17, 18]

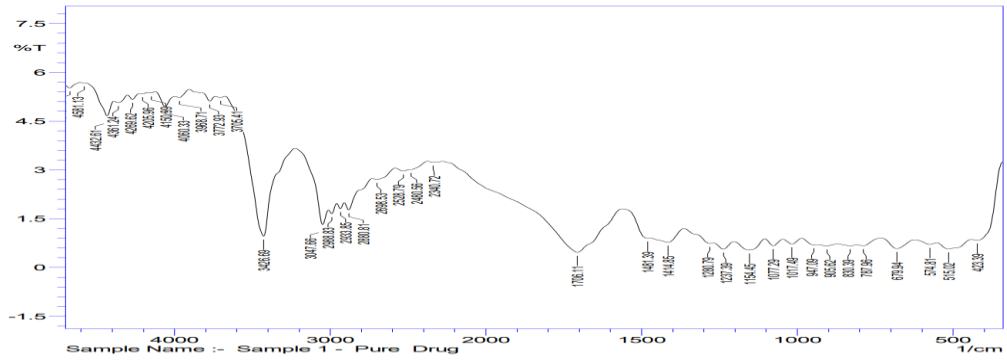
Drug development has come to recognise vitro dissolution as a key component. The information obtained during the research was fitted into the Zero order, First order, Higuchi matrix, Korsmeyer-Peppas, and Hixon Crowell models to analyse the mechanism for the release and rate kinetics of the formulated dosage form. The best-fit model was established by contrasting the r-values obtained.

Stability studies [19]

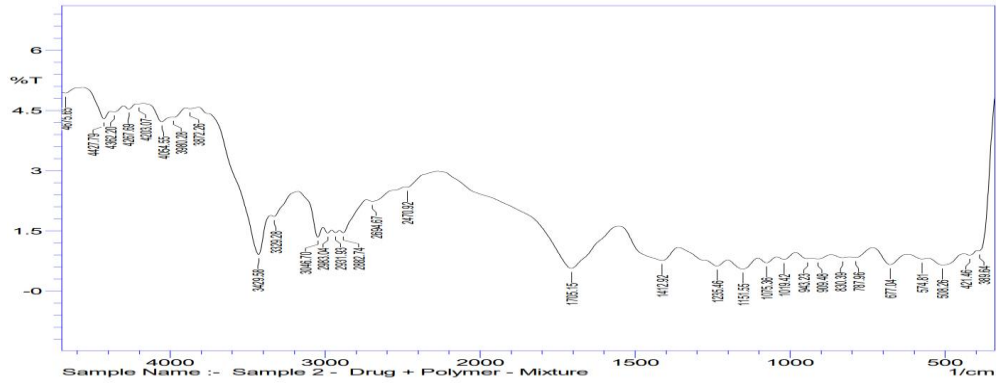
In the present study, stability studies were carried out at (40 ± 2°C / 75 ± 5 % RH), (25°C ± 2°C ,75% ± 5% RH) and (10°C ± 2°C, 75% ± 5% RH) for a specific time period up to 28 days for the optimized formulation. The optimized formulation was analyzed for the drug content study. The optimized formulation was analysed for the drug contents study, lag time (sec), floating time (hours), cumulative drug release (%).

RESULT AND DISCUSSION:

Drug and polymer compatibility studies –



Graph No. 1: FTIR of Rivastigmine Tartrate



Graph No. 2: FTIR of Rivastigmine Tartrate + Polymer

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.

Pre-compression Study –

Table No. 3: Pre – compression study of floating tablet

Batch	Bulk Density (g/cm3 ± SD)	True Density (g/cm3 ± SD)	Carr's Index (% ± SD)	Hausners Ratio (± SD)	Angle of Repose (θ ± SD)
F1	0.553 ± 0.008	0.623 ± 0.012	11.23 ± 0.92	1.12 ± 0.08	31.15 ± 1.31
F2	0.567 ± 0.011	0.642 ± 0.009	11.68 ± 0.68	1.13 ± 0.05	31.75 ± 1.18
F3	0.573 ± 0.003	0.653 ± 0.022	12.25 ± 0.57	1.13 ± 0.07	32.38 ± 1.24
F4	0.557 ± 0.007	0.627 ± 0.008	11.16 ± 0.93	1.12 ± 0.09	33.07 ± 1.43
F5	0.568 ± 0.009	0.648 ± 0.011	12.34 ± 0.73	1.14 ± 0.03	33.69 ± 1.39
F6	0.577 ± 0.013	0.665 ± 0.014	13.23 ± 0.54	1.15 ± 0.04	31.32 ± 1.27
F7	0.564 ± 0.011	0.638 ± 0.021	11.59 ± 0.87	1.13 ± 0.07	32.47 ± 1.13
F8	0.571 ± 0.005	0.653 ± 0.007	12.55 ± 0.92	1.14 ± 0.09	33.02 ± 1.33
F9	0.578 ± 0.009	0.671 ± 0.016	13.85 ± 0.63	1.16 ± 0.05	33.69 ± 1.48

N=3

Bulk density: the bulk density was found in range of 0.553 ± 0.008 - 0.578 ± 0.009 for all formulation batches.
Tapped density: the bulk density was found in range of 0.623 ± 0.012 - 0.671 ± 0.016 for all formulation batches.
Carr's compressibility index: the % compressibility index was found to be in the range of 11.16 ± 0.93 - 13.85 ± 0.63 for all formulation indicating goof flow property.
Housner's ratio: the value of hausner's ratio for all formulation was below 1.15 which indicate good flow property.
Angle of repose: the angle of repose of all formulation were in the range of 31.15 ± 1.13 - 33.69 ± 1.48which show free flow nature of prepared microspheres.

Post compression Study –

Table No. 4 - Post compression study of floating tablet

Batch	Wt. variation (mg ± SD)	Hardness (kg/cm^2 ± SD)	Diameter (mm ± SD)	Thickness (mm ± SD)	Friability (% ± SD)	FLT (Sec ± SD)	TFT (Hour± SD)	Drug Content (% ± SD)
F1	324.54 ± 0.612	5 ± 0.057	9.014 ± 0.154	2.979 ± 0.014	0.41 ± 0.0022	94 ± 0.679	12 ± 0.13	96.89 ± 0.93
F2	324.71 ± 0.553	4.8 ± 0.058	9.013 ± 0.152	2.981 ± 0.017	0.49 ± 0.0019	107 ± 0.559	12 ± 0.11	98.04 ± 0.91
F3	324.60 ± 0.598	5 ± 0.056	9.013 ± 0.159	2.978 ± 0.011	0.48 ± 0.0023	116 ± 0.641	12 ± 0.14	97.46 ± 0.97
F4	324.62 ± 0.549	4.6 ± 0.059	9.014 ± 0.156	2.979 ± 0.008	0.46 ± 0.0025	128 ± 0.631	12 ± 0.09	98.62 ± 0.87
F5	324.70 ± 0.607	4.6 ± 0.058	9.014 ± 0.149	2.979 ± 0.013	0.53 ± 0.0021	106 ± 0.605	12 ± 0.15	97.75 ± 0.94
F6	324.62 ± 0.568	4.8 ± 0.055	9.014 ± 0.157	2.978 ± 0.012	0.44 ± 0.0017	127 ± 0.531	12 ± 0.13	99.77 ± 0.83
F7	324.57 ± 0.544	5± 0.057	9.013 ± 0.155	2.981 ± 0.009	0.47 ± 0.0026	143 ± 0.567	12 ± 0.08	99.19 ± 0.89
F8	324.61 ± 0.537	4.8 ± 0.056	9.012 ± 0.158	2.979 ± 0.015	0.41 ± 0.0024	139 ± 0.614	12 ± 0.11	98.33 ± 0.92
F9	324.52 ± 0.573	5 ± 0.054	9.014 ± 0.151	2.978 ± 0.019	0.54 ± 0.0023	157 ± 0.631	12 ± 0.14	98.9 ± 0.96

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 ± 0.057) kg/cm2. This insures good mechanical strength.

The **Thickness** of all floating tablets was found in the range of (2.978 ± 0.011) to (2.981 ± 0.017) mm. There were no marked variations in the thickness of all formulation indicating uniform behaviour of powder throughout the compression process.

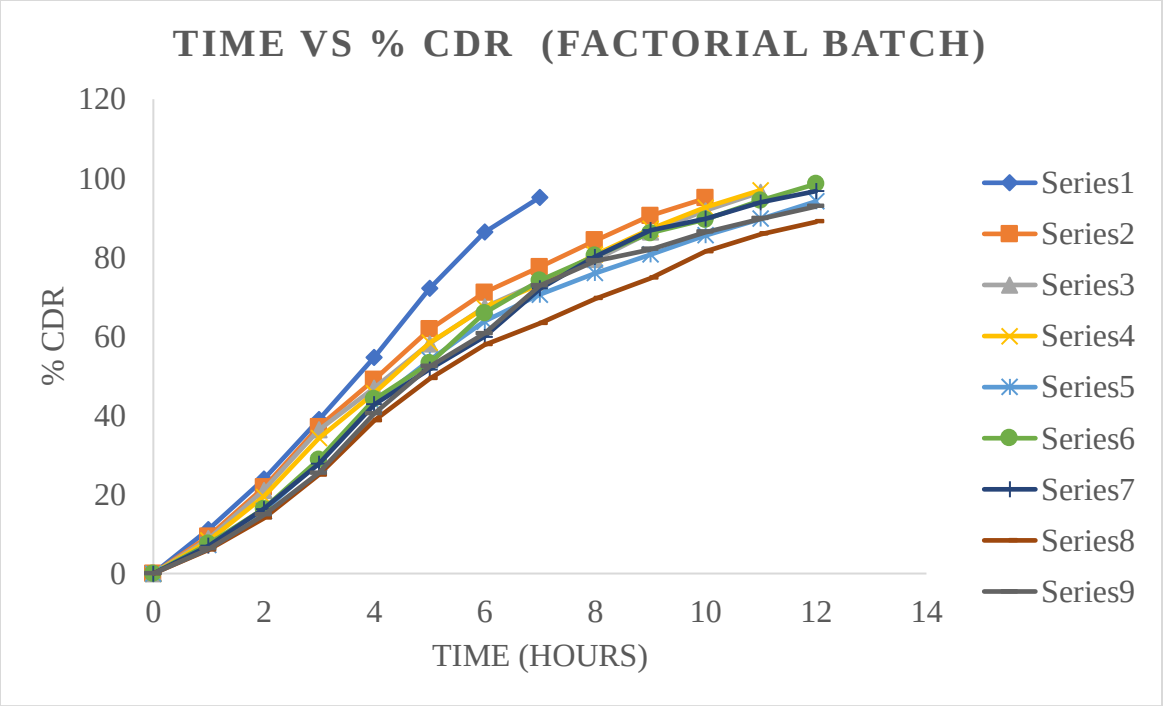
The **Friability** of all floating tablets formulations was in range (0.41 ± 0.0022) to (0.54 ± 0.0023) which indicates the good flow ability.

The **Drug Content** of all formulations was found to be in between (96.89 ± 0.93) to (99.77 ± 0.83) %. The values ensures good uniformity of drug content in the tablet.
From the results it was observed that, **Floating Lag Time (FLT)** of formulations containing sodium alginate as a polymer was in range (94 ± 0.679) to (157 ± 0.631) seconds.

Table No. 5: Dissolution Study (HPMC K4M + Sodium Alginate) –

Time (Hrs)	**% Cumulative Drug Release**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	0	0	0	0
1	11.153 ± 0.181	9.337 ± 0.198	8.818 ± 0.183	8.299 ± 0.175	7.262 ± 0.192	7.521 ± 0.183	7.002 ± 0.167	5.965 ± 0.177	6.224 ± 0.189
2	23.862 ± 0.169	21.787 ± 0.158	21.008 ± 0.171	19.452 ± 0.189	15.821 ± 0.167	16.34 ± 0.188	16.34 ± 0.187	14.006 ± 0.181	14.783 ± 0.173
3	38.905 ± 0.171	37.089 ± 0.163	36.311 ± 0.167	34.236 ± 0.173	28.012 ± 0.183	28.789 ± 0.175	27.752 ± 0.161	24.899 ± 0.193	25.417 ± 0.179
4	54.726 ± 0.191	49.02 ± 0.173	46.945 ± 0.174	45.648 ± 0.198	43.055 ± 0.159	44.092 ± 0.198	42.795 ± 0.173	38.646 ± 0.187	40.461 ± 0.191
5	72.104 ± 0.189	61.729 ± 0.185	58.098 ± 0.181	58.357 ± 0.169	53.948 ± 0.171	53.17 ± 0.154	51.614 ± 0.181	49.28 ± 0.165	52.391 ± 0.183
6	86.369 ± 0.177	71.066 ± 0.178	67.435 ± 0.191	67.175 ± 0.183	63.804 ± 0.177	65.879 ± 0.185	59.914 ± 0.161	57.839 ± 0.176	60.691 ± 0.159
7	95.187 ± 0.161	77.55 ± 0.157	73.659 ± 0.165	73.141 ± 0.159	70.548 ± 0.181	74.178 ± 0.171	72.104 ± 0.154	63.285 ± 0.189	72.881 ± 0.168
8		84.294 ± 0.168	79.366 ± 0.188	80.662 ± 0.169	75.994 ± 0.191	80.403 ± 0.169	80.144 ± 0.188	69.51 ± 0.198	79.106 ± 0.171
9		90.519 ± 0.189	86.368 ± 0.161	87.147 ± 0.171	80.663 ± 0.174	86.109 ± 0.189	86.888 ± 0.177	74.697 ± 0.175	81.959 ± 0.193
10		94.928 ± 0.193	91.815 ± 0.183	92.593 ± 0.193	85.591 ± 0.165	89.481 ± 0.167	89.741 ± 0.183	81.441 ± 0.153	86.368 ± 0.181
11			96.484 ± 0.177	97.002 ± 0.182	89.741 ± 0.192	94.409 ± 0.171	93.89 ± 0.198	85.85 ± 0.188	89.74 ± 0.192
12					94.15 ± 0.188	98.559 ± 0.197	96.744 ± 0.165	88.963 ± 0.175	92.853 ± 0.169

N=3



Graph No. 3: Time Vs. %CDR Floating Tablet

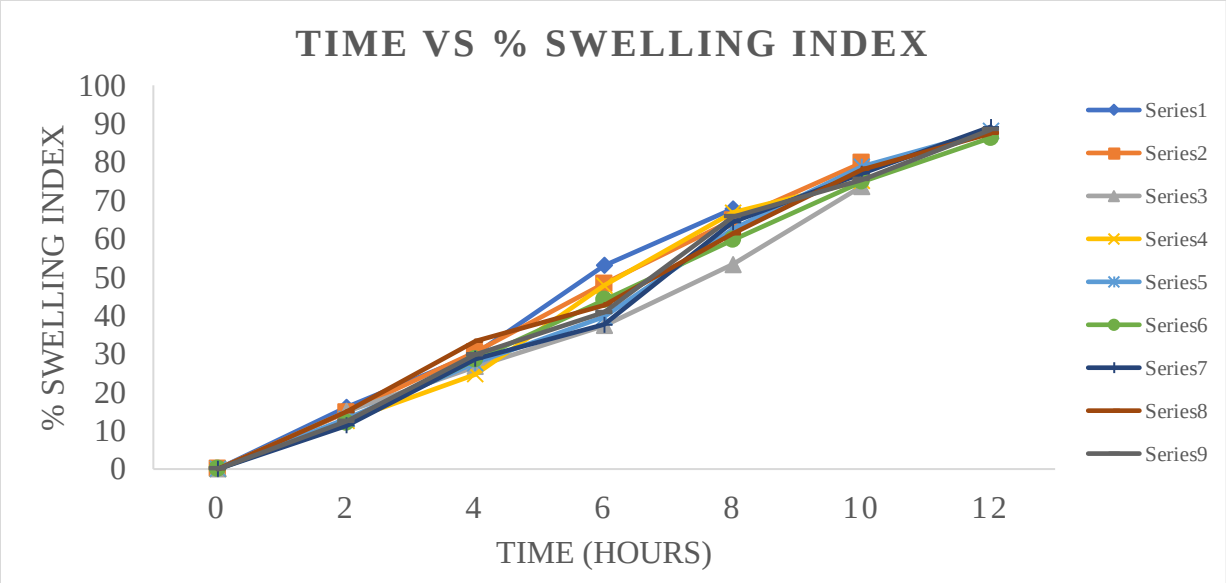
% Cumulative drug release of gastro retentive floating tablets of all the formulations (F1 to F9) was found to be in the range of (5.965 ± 0.177) to (98.559 ± 0.197). It was observed that % cumulative drug release was depend on the concentration of polymers. Here, as the concentration of polymers increases, % drug release time of the formulations decreases. Maximum % cumulative drug release was found to be 98.559 ± 0.197 of F6 Batch.

6.4.4 % Swelling Index

Table No. 6: % Swelling Index of Factorial Batch

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
2	16.08 ± 0.611	14.76 ± 0.813	15.07 ± 0.598	12.61 ± 0.835	13.11 ± 0.705	12 ± 0.873	11.39 ± 0.841	14.97 ± 0.793	12.42 ± 0.786
4	29.93 ± 0.887	30.5 ± 0.839	26.73 ± 0.843	24.69 ± 0.864	27.65 ± 0.856	28.58 ± 0.791	28.71 ± 0.829	33.34 ± 0.872	29.82 ± 0.866
6	53.08 ± 0.864	48.34 ± 0.794	37.39 ± 0.877	47.77 ± 0.857	39.61 ± 0.883	44.04 ± 0.867	37.64 ± 0.789	42.72 ± 0.738	40.81 ± 0.857
8	67.83 ± 0.792	64.85 ± 0.883	53.29 ± 0.792	66.79 ± 0.782	62.48 ± 0.746	59.73 ± 0.858	64.31 ± 0.861	61.31 ± 0.847	65.72 ± 0.832
10		79.81 ± 0.842	73.69 ± 0.867	75.15 ± 0.847	78.86 ± 0.863	74.88 ± 0.753	77.03 ± 0.865	78.04 ± 0.778	75.44 ± 0.798
12					88.21 ± 0.798	86.31 ± 0.858	89.18 ± 0.874	87.46 ± 0.869	88.42 ± 0.887

N=3



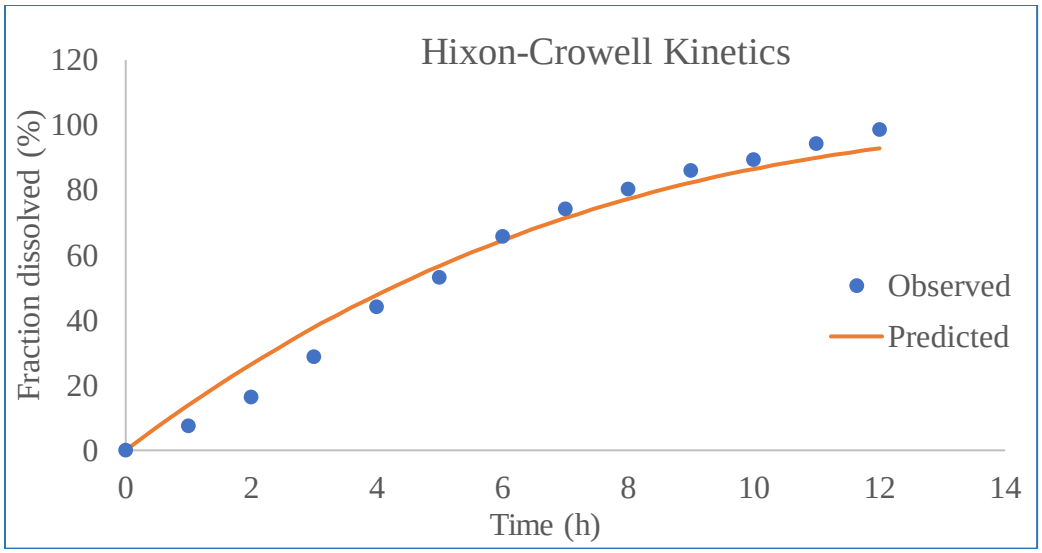
Graph No. 4: Time vs. % Swelling Index

Kinetics Of Drug Release -

Table No. 7: Model Fitting Release Profile Of Floating Tablet Of Rivastigmine Tartrate

Batch	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
	R^2	**R^2**	**R^2**	**R^2**	**R^2**	**R^2**	**R^2**	**R^2**	**R^2**
Zero Order	0.9941	0.9772	0.9627	0.9666	0.9663	0.9615	0.9648	0.9729	0.9524
1st Order	0.9113	0.9603	0.9655	0.9557	0.9544	0.9496	0.9392	0.9661	0.9426
Higuchi Matrix	0.8402	0.9067	0.9182	0.9111	0.8953	0.8940	0.8838	0.8909	0.8780
Hix.Crow	0.9451	0.9846	0.9884	0.9832	0.9799	0.9772	0.9702	0.9852	0.9693
Peppas	0.9964	0.9892	0.9858	0.9858	0.9789	0.9752	0.9736	0.9821	0.9625
n =	1.092	0.840	0.792	0.808	0.835	0.829	0.854	0.856	0.842
Best Fitted	Peppas	peppas	Hix Crow	peppas	Hix Crow	Hix Crow	peppas	Hix Crow	Hix Crow

The value were compared with each other for model based on highest regression value (r), fiiting of the release rate data to the various model revels that the formulation (F1, F2, F4, and F7) have best fitted to peppas model. And F3, F5, F6, F8, and F9 was best fitted to Hix Crow.



Graph No. 5: A plot of Hixon-Crowell kinetics of optimized formulation (F6)

6.4.6 Stability Study –

Table No. 8: Stability study at 40°C ± 2°C / 75 ± 5% RH

Time	% Drug Content	Lag Time (Sec)	Floating Time (Hours)	%CDR After 12 Hrs
0 Days	99.77 ± 0.83	127 ± 0.531	12 ± 0.130	98.559 ± 0.197
1 Weeks	99.75 ± 0.63	127 ± 0.531	12 ± 0.143	98.559 ± 0.176
2 Weeks	99.74 ± 0.71	127 ± 0.531	12 ± 0.256	98.559 ± 0.183
3 Weeks	99.74 ± 0.71	127 ± 0.531	12 ± 0.202	98.559 ± 0.148
4 Weeks	99.74 ± 0.71	127 ± 0.531	12 ± 0.174	98.559 ± 0.192

Table No. 9: Stability study at 25°C ± 2°C / 75 ± 5% RH

Time	% Drug Content	Lag Time (Sec)	Floating Time (Hours)	%CDR After 12 Hrs
0 Days	99.77 ± 0.83	127 ± 0.531	12 ± 0.130	98.559 ± 0.197
1 Weeks	99.75 ± 0.63	127 ± 0.531	12 ± 0.157	98.559 ± 0.171
2 Weeks	99.74 ± 0.71	127 ± 0.531	12 ± 0.244	98.559 ± 0.153
3 Weeks	99.74 ± 0.71	127 ± 0.531	12 ± 0.204	98.559 ± 0.167
4 Weeks	99.74 ± 0.71	127 ± 0.531	12 ± 0.171	98.559 ± 0.182

Table No. 10: Stability study at 10°C ± 2°C / 75 ± 5% RH

Time	% Drug Content	Lag Time (Sec)	Floating Time (Hours)	%CDR After 12 Hrs
0 Days	99.77 ± 0.83	127 ± 0.531	12 ± 0.130	98.559 ± 0.197
1 Weeks	99.75 ± 0.63	127 ± 0.531	12 ± 0.154	98.559 ± 0.164
2 Weeks	99.74 ± 0.71	127 ± 0.531	12 ± 0.241	98.559 ± 0.173
3 Weeks	99.74 ± 0.71	127 ± 0.531	12 ± 0.203	98.559 ± 0.156
4 Weeks	99.74 ± 0.71	127 ± 0.531	12 ± 0.173	98.559 ± 0.178

The performed stability studies of optimised formulation F6 revealed that there is very slight reduction in drug content was observed over the period of 4 weeks. No significant changes were observed in % cumulative drug release after 12 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 (10°C ± 2°C / 75 ± 5% RH). Hence, the optimised formulation F6 was found to be stable for the duration of four weeks.

CONCLUSION:

A 3^2 factorial design was applying for successful preparation of gastro-retentive floating tablet of Rivastigmine Tartrate by direct compression method. The variables HPMC K4M and sodium alginate evaluated in this study as independent variable. It was concluded that, formulation F6 exhibit significant controlled release behaviour for 12 hours and enhanced bioavaibility and reduced dosing frequency and side effects. Hense, F6 formulation batch is concluded as optimized batch as it exhibited significant effect on the responses FLT and % CDR of the formulations.

REFERENCE:

1. Lodh H, Sheeba FR, Chourasia PK, Pardhe HA, Pallavi N. Floating drug delivery system: A brief review. Asian Journal of Pharmacy and Technology. 2020 Nov 18;10(4):255-64.
2. Jain N. K., Advances in controlled and novel drug delivery. New Delhi: CBS publisher and distributors. 2008; 4: 11- 21.
3. Raza M, Jayswal MG, Ahmed A, Majaz Q, Khan GJ. REVIEW ON GASTRO RETENTIVE DRUG DELIVERY SYSTEM.
4. Rivastigmine tartrate [Internet]. Trc-canada.com. 2019 [cited 31 March 2019]. Available from: https://www.trc-canada.com/prod-img/MSDS/R541000MSDS.pdf
5. Jadi RK, Bomma R, Sellappan V. Development of a new single unit dosage form of propranolol HCl extended release non-effervescent floating matrix tablets: In vitro and in vivo evaluation. Journal of Applied Pharmaceutical Science. 2016 May 28;6(5):112-8.
6. Jadi RK, Bomma R, Sellappan V. Development of a new single unit dosage form of propranolol HCl extended release non-effervescent floating matrix tablets: In vitro and in vivo evaluation. Journal of Applied Pharmaceutical Science. 2016 May 28;6(5):112-8.
7. Chatwal RG, Anand KS. Instrumental methods of chemical analysis. 5th ed. Mumbai: Himalaya Publishing House; 2014.
8. Banker, Gilbert S. "The theory and practice of industrial pharmacy". Vol. 1. Edited by Leon Lachman, Herbert A. Lieberman, and Joseph L. Kanig. Lea Febiger, Philadelphia, (1970): 1531-1531.
9. Kukati L, Chittimalli K, Shaik NB. Formulation and evaluation of floating tablets of cefpodoxime proxetil. Journal of scientific research. 2014 Aug 26;6(3):563-79.
10. Shilpa BC, Vishnu P, Babu KN, Rao UK, Sai S, Saravani T. A brief review on floating drug delivery system. S Pac J Pharm Bio Sci. 2014;2:137-53.
11. Mayavanshi AV, Gajjar SS. Floating drug delivery systems to increase gastric retention of drugs: A Review. Research Journal of Pharmacy and Technology. 2008 Oct;1(4):345-8.
12. Sutar FY, Gangurde AB, Patil DM. A Scientific Review On: Floating Drug Delivery System (FDDS). IJPRS. 2014;3(3):297-314.
13. Patel SS, Ray S, Thakur RS. Formulation and evaluation of floating drug delivery system containing clarithromycin for Helicobacter pylori. Acta Pol Pharm. 2006 Jan1;63(1):53-61.
14. Tanwar YS, Jamini M, Srivastava B. Formulation and in vitro evaluation of floating tablets of Losartan potassium. Mahidol University Journal of Pharmaceutical Sciences. 2013;40(2):17-24.
15. Padmavathy J, Saravanan D, Rajesh D. Formulation and evaluation of ofloxacin floating tablets using HPMC. International journal of pharmacy and pharmaceutical sciences. 2011;3(1):170-3.
16. Kumar R, Patil MB, Patil SR, Paschapur MS. Formulation and evaluation of effervescent floating tablet of famotidine. Int J Pharm Tech Res. 2009 Jul;1(3):754-63.
17. Aulton M. The Science of Dosage Form Design. 2nd Edition, Churchill Livingstone, Hungary, 2008: 111 & 310.
18. Dash S, Murthy PN, Nath L, Chowdhury P. Kinetic modeling on drug release from controlled drug delivery systems. Acta Pol Pharm. 2010 May 1;67(3):217-23.
19. Danki LS, Sayeed A, Kadam S, Salger S. Research Journal of Pharmaceutical, Biological And Chemical Scienes. vol. 2010 Sep;1:108-30.