


Preparation and Evaluation of Sustained Release Tablets of Valacyclovir

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ABSTRACT

Valacyclovir HCL is a prodrug of acyclovir that is metabolically activated and inhibits viral DNA replication. It is used to treat and/or prevent certain types of herpes simplex virus (HSV type-1 and HSV type-2) infections, including genital herpes (genital sores) and cold sores (orolabial sores). Valacyclovir is BCS class-III. Drug (high solubility and low permeability). More specifically, it is appreciated that SR formulations are generally designed to release the drug slowly over time and gradually absorb into the upper small intestine. Valacyclovir SR Tablets should be administered twice daily at a dose of 500mg to maintain therapeutically appropriate blood levels of the active ingredient. The aim of the present investigation was to prepare, characterize and evaluate oral sustained release Tablets Valacyclovir to improve adherence and thereby improve efficacy and patient compliance.

KEYWORDS: Valacyclovir; Cross povidone; Sodium Starch Glycolate; Direct Compression Method; Optimization Center Mixture Design.

1. INTRODUCTION

A properly designed controlled release dosage form is advantageous over a regular release dosage form by desirably delivering a therapeutic dose of the drug over a longer period of time, which elicits a pharmacological effect at a lower dose and consequently reduces unwanted adverse effects. Oral route is preferred for drug delivery because of its ease of administration, better patient compliance and flexibility in formulation, making an oral controlled release Tablet a complex task. Gastrointestinal tract. Considerable efforts have been made to design orally controlled drug delivery systems that produce more predictable and increased bioavailability of drugs¹. In some situations, prolonging the gastric residence of the drug is advantageous to achieve greater therapeutic effects, e.g., G.I. Drugs that are absorbed proximally, act locally in the stomach, and are poorly soluble or degraded. Alkaline pH. Recent approaches implemented to increase the gastric residence time of drug include bio adhesive system, swelling system, low or high density system, magnetic system, non-collapsible system and superfine biodegradable hydrogel system. Insights into formulation technology, a low-density floating drug delivery system is a logical approach² but is only effective when the volume of fluid in the stomach is high enough, and if the stomach is drained, the flotation of the dosage form is impeded³. Gastric emptying of floating dosage forms can occur randomly in the supine individual and depends on the diameter. The swelling approach requires sufficient time for proper expansion of the dosage form and is likely to be swept from the pylorus until it swells. A combination of two or more gastric indwelling approaches is best in gastric retention practice, e.g., swelling and flotation, swelling and bioadhesive, swelling and high-density structure, and bioadhesive and high-density structure. Therefore, to overcome the disadvantages of both gastric blocking approaches, a combination of bloat and floating approach is used and is expected to be better for gastric retention than a single one. This combination is advantageous through reduction of dose and dosage regimen and reduction of side effects, and increases patient compliance by increasing drug absorption and

bioavailability. Acyclovir and valacyclovir are antiviral agents used in the treatment of herpes simplex and herpes zoster infections. Valacyclovir hydrochloride is a prodrug of acyclovir with higher solubility and bioavailability (about 54%) than acyclovir. However, valacyclovir hydrochloride is not absorbed from the colon [18]. It is absorbed from the upper part of the small intestine by an active transport mechanism. Valacyclovir HCl is chemically more stable at the acidic pH of the stomach (below 4). Therefore, a gastric barrier dosage form is a good approach for valacyclovir hydrochloride. Also, it has a short biological half-life of 2.5-3.3 hours, so effective drug therapy requires frequent administration of the drug to a patient. Therefore, the efficacy of medical treatment can be enhanced by providing sustained drug delivery with gastro destination. Consequently, to develop and evaluate a sustained-release Tablet of Valacyclovir HCl using polyethylene oxide as anti-inflammatory and anti-floating gastritis.

2. MATERIALS AND METHODS

2.1. MATERIALS

Valacyclovir was obtained from Pharmaceuticals and Chemicals, Strides Pharmaceutical Sciences. Cross Povidone and Sodium Starch Glycolate ST Fine Chemicals Pvt Ltd, Bangalore, Microcrystalline Cellulose and Sodium Bicarbonate, Central Drug House Pvt Ltd, Delhi, Citric Acid and Magnesium Stearate at Sigma Aldrich Chem. Bangalore.

2.2. METHODS

2.2.1. Preparation of Tablets

Each floating Tablet containing 500 mg valacyclovir HCl is prepared by direct compression method, super disintegrating sodium starch glycolate, cross povidone swelling matrix, sodium bicarbonate as gas forming agent and sodium starch glycolate (SSGlation) enhancer. Valacyclovir HCl API and excipients were accurately weighed through a 40 # sieve. API, Cross povidone SSG, sodium bicarbonate and MCC were mixed in a mortar and pestle. The above mixture was passed through 18 # sieve to break the agglomeration and further mixed. The above mixture is lubricated with magnesium stearate for 4-5 minutes before compression. Then, the mixture was compacted using 12.6 concave facing round punches in a single-station compaction machine.

3. EVALUATION

3.1 Determination of melting point:

The melting point of valacyclovir was determined by the capillary method. Valacyclovir fine powder was filled into a glass capillary tube (previously capped at one end). The capillary tube is connected to the thermometer and the thermometer is placed in a tube containing liquid paraffin. The assembly was placed on an oil bath (burner) and allowed to gradually increase in temperature. The melting temperature of the powder was observed. Triplicates of measurements taken and averaged are reported (n=3).

3.2 Compatibility study:

Fourier transform infrared spectroscopy (FTIR) is used to verify compatibility interactions between drug and excipients. FTIR spectra of drug and excipient mixtures were compared with FTIR spectrum of pure drug.

3.3 Preparation of Standard Curve of Valacyclovir in 0.1N Hydrochloric Acid

100mg of Valacyclovir was completely dissolved in 0.1N HCL after sonication in a 100ml volumetric flask, which was called stock solution-I. 1000 µg/ml 2.5 ml stock solution-I was diluted to 25 ml using 0.1N hydrochloric acid solution, called stock solution. 100µg/ml II. Serial dilutions of this stock solution-II were made to obtain drug solutions at concentrations ranging from 3, 6,9,12,15,18,21, 24, 27, 30 & 33 µg/ml. The absorbance of the solutions was measured at 252 nm using a UV-visible spectrophotometer. The procedure was repeated three times and the mean measurements were considered. A graph of concentration v/s absorbance is plotted.

3.4 Pre-formulation studies

The prepared powder mixture was evaluated by its flow ability and compressibility angle, Carr's index and Hauser's ratio.

3.5 Post-formation studies

The prepared Tablets are evaluated for hardness (Monsanto hardness tester), thickness, friability, weight variation and % assay resolution.

Other studies include drug and excipient compatibility, % swelling or % water absorption study, test flotation lag time or flotation time, test drug dissolution and release kinetics and total flotation time.

3.6 % Swelling or % Water Absorption Studies:

The swelling state of the polymer is considered critical for its muco adhesive behavior. To determine the swelling index, weighed Tablets were placed on glass slides and then these glass slides were placed in Petri

dishes containing 20 ml of 0.1 N HCl so that the upper surface of the Tablet was immersed in the liquid medium. The glass slides were taken out at regular intervals, excess moisture was removed and the Tablets were reweighed. The following formula was used to determine the swelling index, where Wt = weight of Tablet at time t, and Wo = weight of Tablet at time 0. This can be multiplied by 100 to get the result in percentage terms.

$$\% \text{Swelling} = \frac{W_t - W_o}{W_o} \times 100$$

The percentage of swelling of the Tablet is expressed as the percentage of water absorption (% WU), where Wt = weight of swollen Tablet and Wo = initial weight of Tablet

3.7 *In-vitro* flotation determination

The floating behaviour of the Tablet was determined using USP dissolution apparatus-II in 500 ml of 0.1 N HCl, maintained at 37 ± 0.5 °C, rotated at 50 rpm. Float delay time and total float time are observed

3.8 *In-vitro* dissolution study

The Tablet was introduced into the dissolution test apparatus and the apparatus was set at 50 rpm. At sampling time intervals 5 mL of sample was withdrawn and replaced with 5 mL of 0.1N HCL solution. The withdrawn samples were diluted in both 10 ml or 50 ml according to the concentration of the drug. Diluted samples were analysed by UV spectra-photometer at 252 nm. Each formulation was tested for dissolution of 3 Tablets and the average was calculated using 0.1N HCL solution as blank.

4. Optimization studies:

Optimization by DOE to find the values of the controllable independent variables that give the most desired value of the dependent variable. The most popular response surface method designs (RSM) is the central composite design (CCD), also known as the Petty-Wilson design, which is often used for second-order models. A central composite design is based on a two-level factorial design with (2n) axis or star points (2n) and a central point suitable for quadratic models. Thus the total number of factor combinations in a CCD is given by 23 central composite design and plotted with 2 quantitative numerical factors (ie, concentration of sodium bicarbonate, & concentration of super disintegrants) and 1 qualitative categorical factor (ie, Level 1 of C). , & position 2 of C) is selected. Among the 2 numerical factors mentioned are maximum (+1), minimum (-1) and medium concentration and qualitative/categorical factors such as concentration of sodium bicarbonate and concentration of super disintegrants. I.e. amount of gross povidone & amount of sodium starch glycolate). All other formulations and processing factors were kept constant throughout the study. % drug release (4th hour & 10th hour), total flotation time, flotation lag time, % swelling respectively. Marked (low/high) center points were selected at all stages. A focal point was replicated to provide better predictive capability. A total of 18 experiments were plotted near the center of the factor space, with a face-centered central mixed design considering medium concentration.⁶

The linear model was found for 4th hour drug release when analysed with ANOVA with p-value 0.0020 and R² value 0.6407 showing model is significant. In 10th hour release the model suggested was linear with p-value < 0.0001 and R² value 0.5345 showing model is significant. For swelling index p value was recorded the <0.0001 and R² 0.9946 showing model is significant. The linear models are used for this all responses. During optimization, the goals were applied in range to both factors and response. The factors were in the range of 4(lower limit) and 12(upper limit) and the responses were in the range of 0.30(lower limit) and 1.32(upper limit) for floating lag time and 8.69. (Lower limit) and 44.2 (upper limit) for 4th hour drug release, 28.7(lower limit) and 98.54 (upper limit) for 10th hr drug release and 11 (lower limit) and 12 (upper limit) for floating duration time. And 102.38(lower limit) and 261.47 (upper limit) for % swelling, Based on the analysis of the responses by ANOVA and goals applied in range to both factors and responses, the possible solutions were obtained in order of desirability. One optimum formulations (FB13) were selected by intensive search performed over the entire experimental domain, to validate the chosen experimental design and polynomial equations and further optimized with the help of model graphs.

Graphical depiction of the mathematical relationship is known as response surface. A response surface plot is a 3-D graphical representation of a response plotted between two independent variables and one response variable. The use of 3-D response surface plots allows understanding of the behavior of the system by demonstrating the contribution of the independent variables.

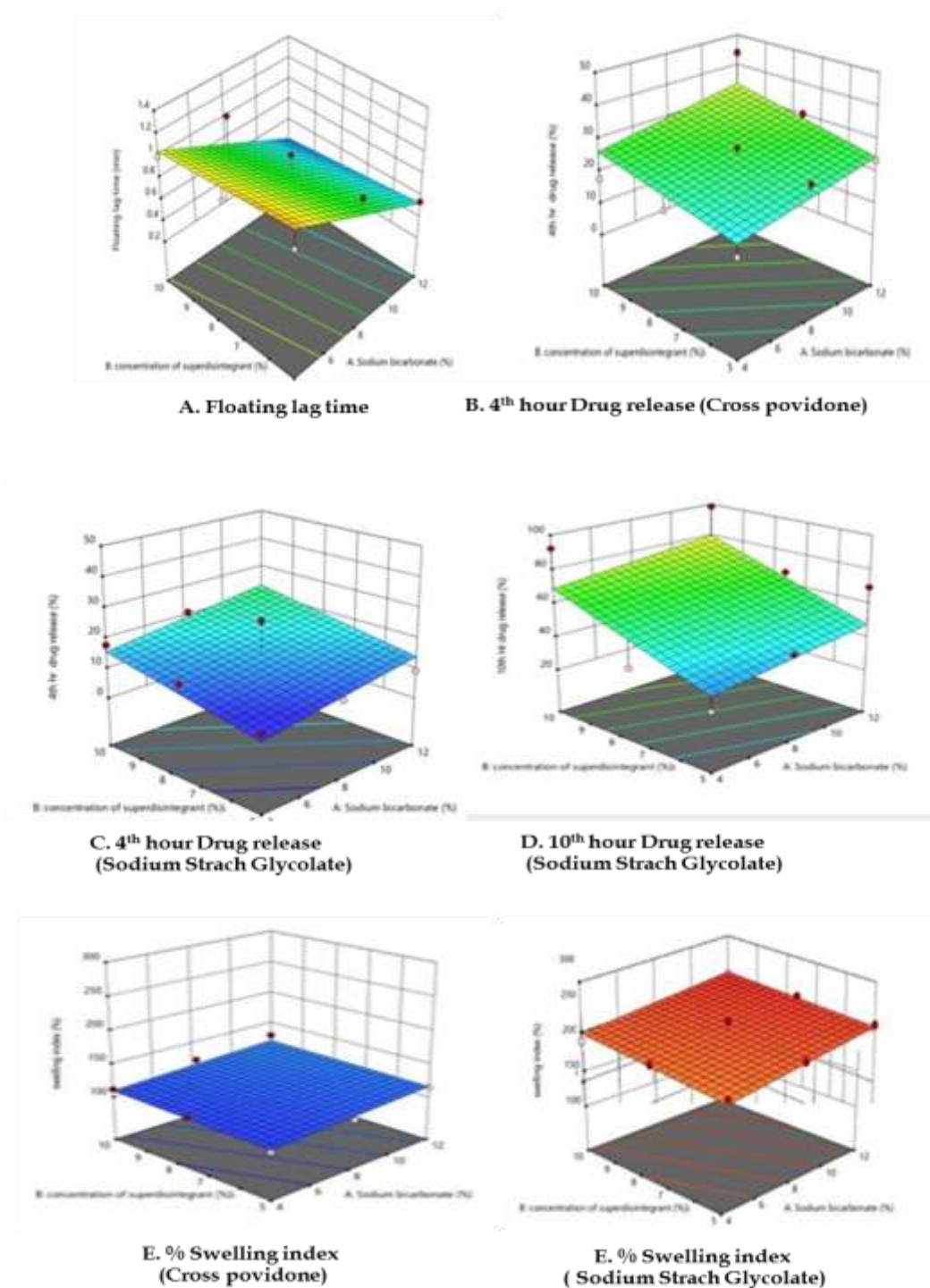


Figure 6. Optimization studies

5. RESULTS AND DISCUSSION

5.1. Determination of Melting point:

Melting point of Valacyclovir was determined by capillary method. The melting point of Valacyclovir was found to be 252°C, which is in accordance with the literature.

5.2. Compatibility study:

FTIR techniques have been used here to study the physical and chemical interaction between drug and excipients used. Compatibility studies were performed using FTIR spectrophotometer. The FTIR spectrum of pure drug and physical mixture of drug and super disintegrants were studied. The characteristic absorption peaks of Valacyclovir were obtained which is abbreviated in **Figure 1**

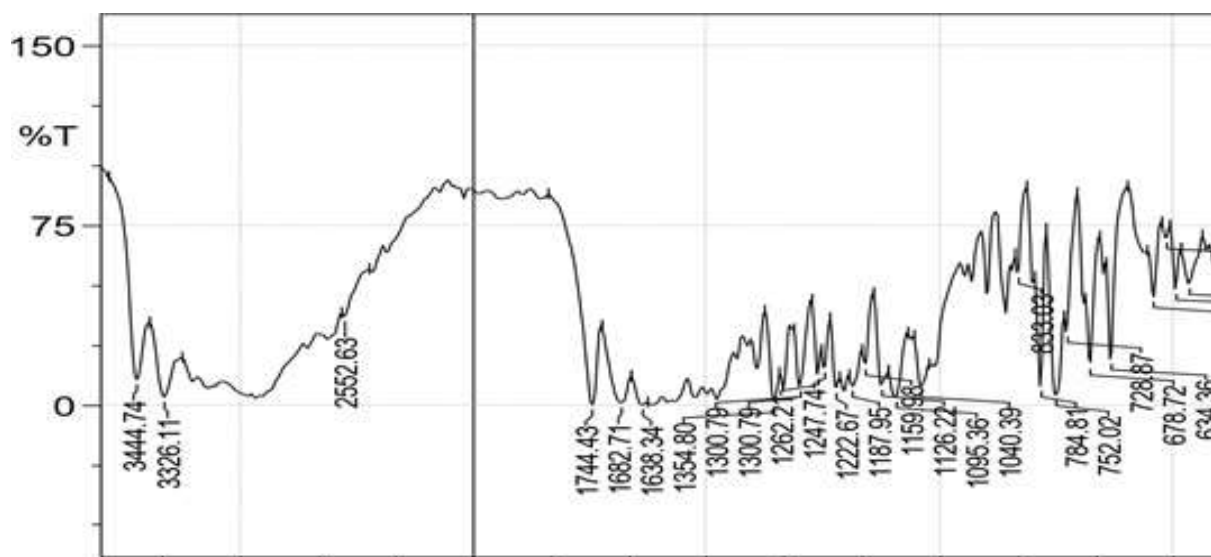


Figure 1. FTIR Spectra of Valacyclovir

5.3. Preparation of Standard Curve of Valacyclovir in 0.1N Hydrochloric acid

The Standard calibration curve of Valacyclovir was developed at 252nm. The calibration curve was linear between 3-33 $\mu\text{g/ml}$ concentration ranges in 0.1N HCL solution. The R^2 and slope were found to be 0.9938 and 0.03465 respectively. The results were shown in Table 1 & Figure 2.

Table 1. Calibration curve of Valacyclovir in 0.1N HCL

Concentration ($\mu\text{g/ml}$)	Absorbance
0	0
3	0.127 \pm 0.05
6	0.204 \pm 0.090
9	0.302 \pm 0.0131
12	0.405 \pm 0.0175
15	0.500 \pm 0.0215
18	0.638 \pm 0.0276
21	0.691 \pm 0.0300
24	0.798 \pm 0.0345
27	0.935 \pm 0.0404
30	1.005 \pm 0.0438
33	1.207 \pm 0.0521

5.4. Pre-formulation studies:

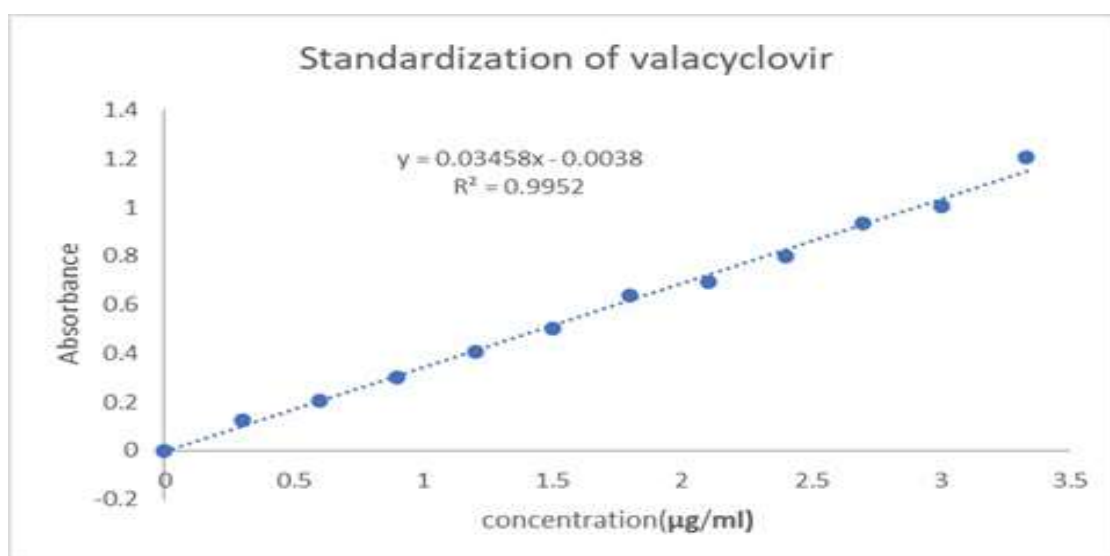


Figure 2: Standard curve of Valacyclovir by using 0.1N HCL

The all Pre formulation studies are results are shown in the Table2, the all preformulations are showed good and excellent flow property.

Table 2. Pre formulation parameters results.

Formulations	Angle of repose (θ)	Tapped density (wt/vol)	Bulk density (wt./vol)	Hausner's ratio	Carr's Index %
F1	22.52	0.81	0.75	1.08	7.4
F2	23.45	0.78	0.72	1.08	7.6
F3	26.20	0.80	0.73	1.09	8.7
F4	22.54	0.78	0.72	1.08	7.6
F5	23.24	0.79	0.73	1.08	7.5
F6	25.32	0.80	0.74	1.08	7.5
F7	24.25	0.78	0.71	1.08	8.9
F8	26.25	0.78	0.72	1.08	7.6
F9	25.28	0.80	0.74	1.11	7.5
F10	26.14	0.81	0.74	1.09	8.6
F11	25.41	0.82	0.75	1.09	8.5
F12	24.56	0.79	0.73	1.09	7.5
F13	23.41	0.78	0.72	1.09	8.6
F14	22.35	0.81	0.74	1.09	8.6
F15	23.24	0.80	0.74	1.08	7.5
F16	24.45	0.81	0.75	1.09	7.4
F17	25.26	0.80	0.75	1.08	6.2
F18	24.54	0.82	0.76	1.08	7.5

5.5. Post formulation study: After completion of pre formulation studies, the post formulations studies are conducted these results are shown in the Table3.

Table 3. Post formulation studies results

Formulations code	Thickness (mm) n=3	Weight of Tablets (gm) n=3	Hardness (kg/cm ²) n=3	Friability (%)	Assay (%)
FB1	6.5±0.02	0.82±0.015	7-8	0.0125	96.25±0.74
FB2	7.18±0.03	0.81±0.022	7-8	0.0124	97.2±0.94
FB3	7.3±0.04	0.79±0.017	7-8	0.0125	99.5±0.58
FB4	7.2±0.014	0.81±0.031	7-8	0.0123	96.25±0.65
FB5	7.3±0.015	0.80±0.015	7-8	0.0124	98.56±0.74
FB6	6.5±0.014	0.795±0.018	7-8	0.0124	99.25±0.52
FB7	7.3±0.012	0.80±0.017	7-8	0.0123	96±0.75
FB8	6.6±0.011	0.81±0.015	7-8	0.0124	100.25±0.24
FB9	6.8±0.010	0.812±0.018	7-8	0.0122	98.41±0.54
FB10	7.3±0.02	0.79±0.017	7-8	0.0124	99.74±0.62
FB11	6.9±0.03	0.80±0.017	7-8	0.0122	101.47±0.51
FB12	7.5±0.04	0.80±0.015	7-8	0.0123	99.47±0.23
FB13	7.3±0.014	0.79±0.015	7-8	0.0124	97.14±0.21
FB14	7.2±0.015	0.80±0.018	7-8	0.0125	98.27±0.24
FB15	7.3±0.014	0.79±0.017	7-8	0.0125	99.47±0.47
FB16	7.1±0.012	0.80±0.017	7-8	0.0123	100.2±0.58
FB17	7.2±0.011	0.81±0.015	7-8	0.0124	99.24±0.57
FB18	7.3±0.010	0.80±0.018	7-8	0.0124	98.33±0.34

5.6. %Swelling:

The % swelling index for all formulation was found to be 108.38% to 261.47% of Valacyclovir 500 mg Tablet. The results were shown in Table 4

Table 4: Results for % Swelling

Formulation code	% swelling					
	1h	2h	3h	4h	5h	6h
FB1	17.06	34.12	51.19	68.25	85.32	102.38
FB2	22.08	41.43	73.28	80.82	92.63	115.06
FB3	6.66	24.10	34.18	38.80	54.18	111.96
FB4	5.28	23.50	45.48	70.35	91.48	129.13
FB5	4.43	33.95	44.1	79.86	91.46	108.87
FB6	4.79	25.5	44.00	78.42	92.63	109.76
FB7	23.28	41.26	71.23	72.9	92.46	105.47
FB8	11.26	15.18	23.03	40.78	74.40	122.18
FB9	2.55	23.50	51.27	78.19	102.55	112.09
FB10	51.71	113.18	153.08	217.46	229.10	250.17
FB11	51.02	88.08	126.10	175.42	220.32	258.53
FB12	50.68	77.51	106.46	159.18	200.17	242.68
FB13	54.01	113.33	164.44	211.45	251.11	258.80
FB14	47.52	70.5	112.82	160.51	220.68	249.91
FB15	40.92	78.76	114.55	158.73	215.411	260.44
FB16	54.60	109.04	171.16	203.41	233.61	252.55
FB17	50.766	74.61	117.71	148.04	222.82	246.50
FB18	40.75	73.80	112.5	170.37	212.5	261.47

5.7. In-vitro buoyancy time:**Floating lag time: 7**

The floating lag time for all formulation was found to be 0.30 mins to 1.32 mins of Valacyclovir 800 mg Tablet. The results were shown in Table 5

Total floating time:

The total floating time for all formulation was found to be 11 to 12 hrs of Valacyclovir 800 mg Tablet.

The results were shown in Table 5

Table 5. In-vitro buoyancy time

Formulation	Floating lag time (In seconds)	Total floating time (In hours)
FB1	60	12
FB2	55	12
FB3	60	12
FB4	30	12
FB5	30	12
FB6	30	12
FB7	60	12
FB8	60	11
FB9	60	12
FB10	60	12
FB11	32	12
FB12	58	11
FB13	30	12
FB14	92	12
FB15	35	12
FB16	65	11
FB17	65	12
FB18	70	12

5.8. The In-vitro dissolution study:

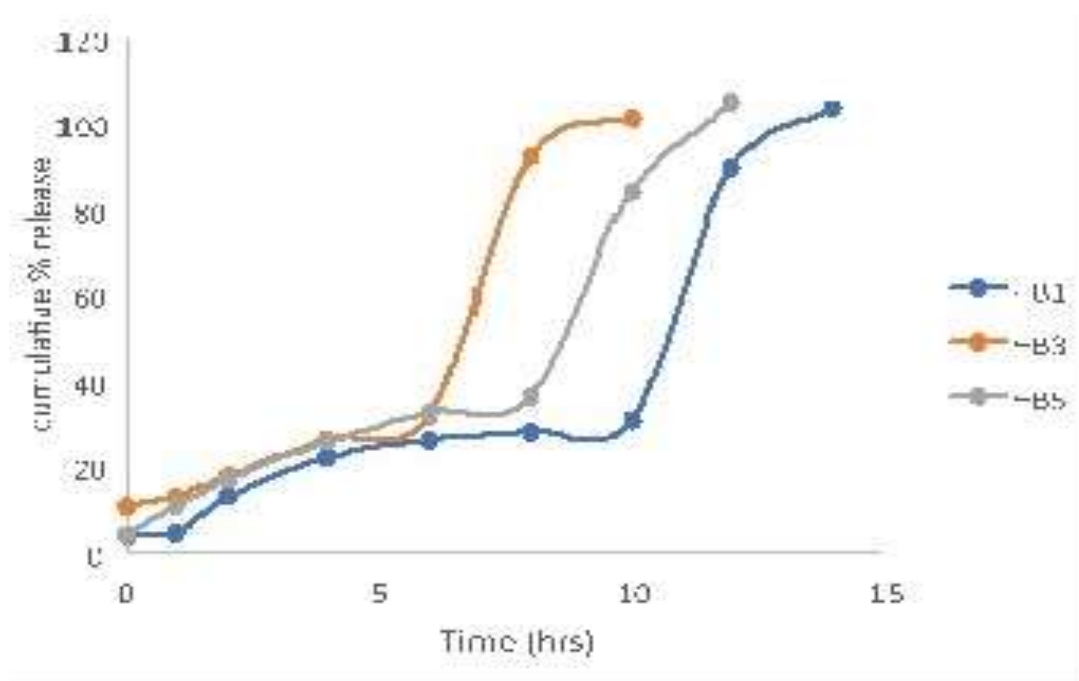
From these readings it can be concluded that floating lag time depends upon amount of Sodium bicarbonate. The more % of sodium bicarbonate lesser will be floating lag time. Time for drug release controlled by % of super disintegrants, greater the % super disintegrant shorter will be time for complete drug release.

Table 6. The *In-vitro* dissolution study:

Formulation	Time (hrs)	0	1	2	4	6	8	10	12	14	16	18
→												
FB1	0	3.83±1.	4.3±1.2	13.2±1.1	22.1±1.	26.1±1.	28.1±	30.08±	89.82±	103.4±1	100.2±	
	25		1	0	10	05	1.23	1.10	1.02	.25	1.09	
FB2	0	4.3±1.0	19.16±1	23.5±1.1	27.80±1	46.83±1	69.94±	104.4±	95.21±	--	-	
	2		.19	2	.12	.08	1.22	1.19	1.22			
FB3	0	10.6±1.	13.02±1	17.79±1.	26.30±1	31.69±1	92.4±	101.27	99.45±	-	-	
	20		.28	12	.25	.10	1.02	±1.22	1.02			
FB4	0	28.4±1.	37.12±1	44.2±1.1	46.29±1	46.72±1	98.54±	104.5±	100.47	-	--	
	05		.15	0	.18	.45	1.03	1.20	±1.24			
FB5	0	4.11±1.	10.70±1	17.04±1.	25.97±1	32.50±1	36.22±	84.15±	104.80	87.41±1	-	
	04		.11	14	.21	.22	1.25	1.21	±1.25	.23		
FB6	0	16.3±1.	23.91±1	30.6±1.1	36.13±1	39.61±1	67.38±	94.33±	102.25	92.48±1	--	
	5		.21	5	.17	.55	1.22	1.23	±1.22	.14		
FB7	0	3.86±1.	21.28±1	24.99±1.	26.71±1	28.7±1.	44.1±	96.04±	103.03	88.14±1	---	
	2		.21	21	.22	02	1.11	1.14	±1.14	.26		
FB8	0	4.97±1	26.26±1	36.16±1.	38.04±1	44.15±1	58.91±	101.96	85.10±	--	--	
			.28	47	.15	.15	1.10	±1.24	1.13			
FB9	0	4.44±1.	23.77±1	27.33±1.	31.44±1	33.37±	44.17±	77.47±	102.50	85.32±10	--	
	03		.22	17	.18		1.09	1.21	±1.11	24±		
FB10	0	3.49±1.	4.52±1.	8.69±1.2	16.34±1	23.76±1	29.10±	35.87±	69.90±	100.7±1	89.45±	
	00		20	2	.09	.02	1.08	1.20	1.10	.24	1.22	
FB11	0	3.83±1.	4.16±1.	9.26±1.1	18.79±1	25.59±1	36.07±	50.49±	60.52±	88.83±1	103.82	
	04		20	7	.9	.22	1.08	1.13	1.04	.23	±1.18	
FB12	0	4.5±1.0	9.3±1.2	17.88±1.	30.74±1	36.52±1	76.57±	103.23	100.54	--	--	
	6		8	21	.7	.04	1.15	±1.14	±1.08			
FB13	0	4.18±1.	6.76±1.	13.57±1.	24.77±1	31.05±1.4	56.32±	76.86±	100.25	85.45±1	--	
	00		22	21	.5		1.14	1.24	±1.25	.03		
FB14	0	3.42±1.	4.41±1.	14.12±1.	20.5±1.	33.25±1	36.55±	71.51±	103.08	85.24±1	--	
	25		22	12	41	.10	1.12	1.12	±1.25	.24		
FB15	0	3.11±1.	3.9±1.1	13.96±1.	20.98±1	29.81±1	37.84±	53.11±	105.43	78.54±1	--	
	03		9	14	.12	.24	1.14	1.09	±1.21	.22		
FB16	0	2.9±1.0	3.8±1.1	9.01±1.1	25.5±1.	32.56±1	37.52±	71.03±	91.880	102.69±	78.58±	
	4		6	25	.22	.22	1.21	1.05	±1.01	1.20		
FB17	0	13.97±1	17.18±1	21.05±1.	32.91±1	37.51±1	66.15±	104.31	84.54±	--	--	
	.05		.08	18	.12	.20	1.14	±1.04	1.10			
FB18	0	9.76±1.	18.89±1	26.00±1.	33.14±1	34.14±1	37.12±	67.75±	102.30	88.25±1	--	
	23		.18	02	.22	.25	1.22	1.22	±1.04	.01		

Standard graphs for cumulative % Drug release:

In Cumulative % drug release the graphs are drawn the Sodium bicarbonate as constant values vs different concentrations of Suiper disintegrants.

**Figure 3. Graph Showing Cumulative % Drug Release Vs time for FB1, FB3,FB5.**

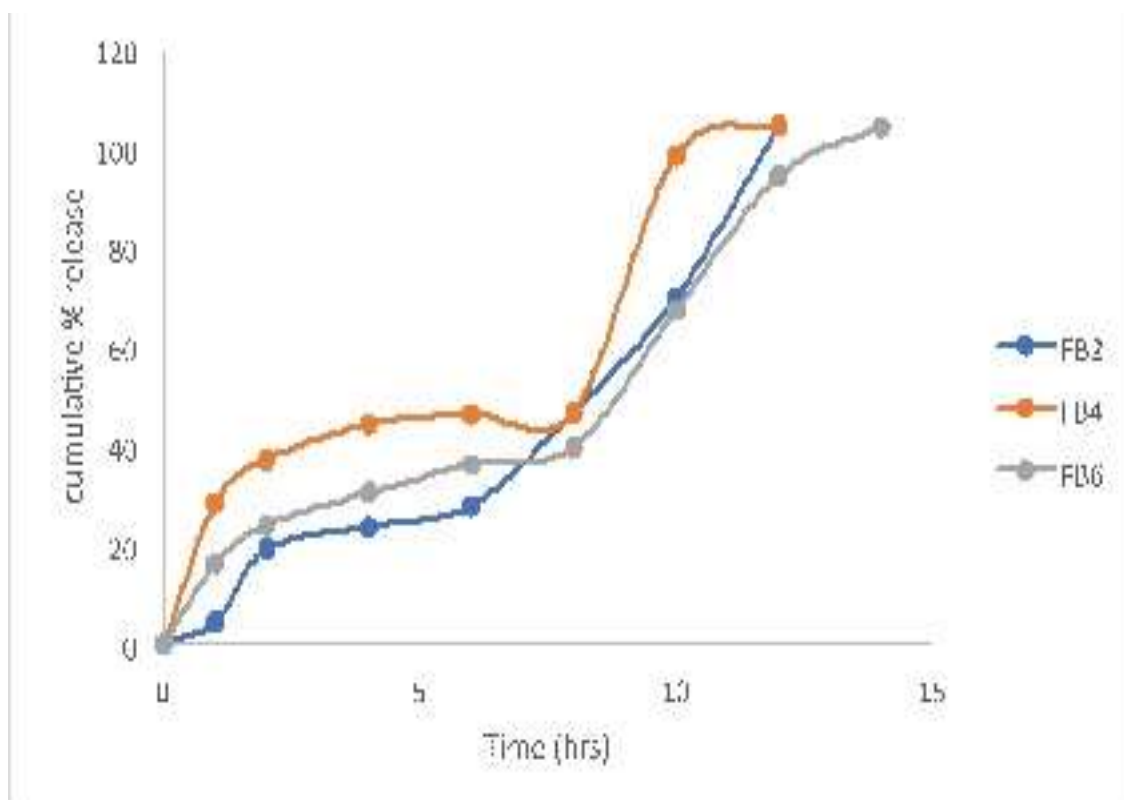


Figure 4. Graph Showing Cumulative % Drug Release Vs time for FB2, FB4,FB6.

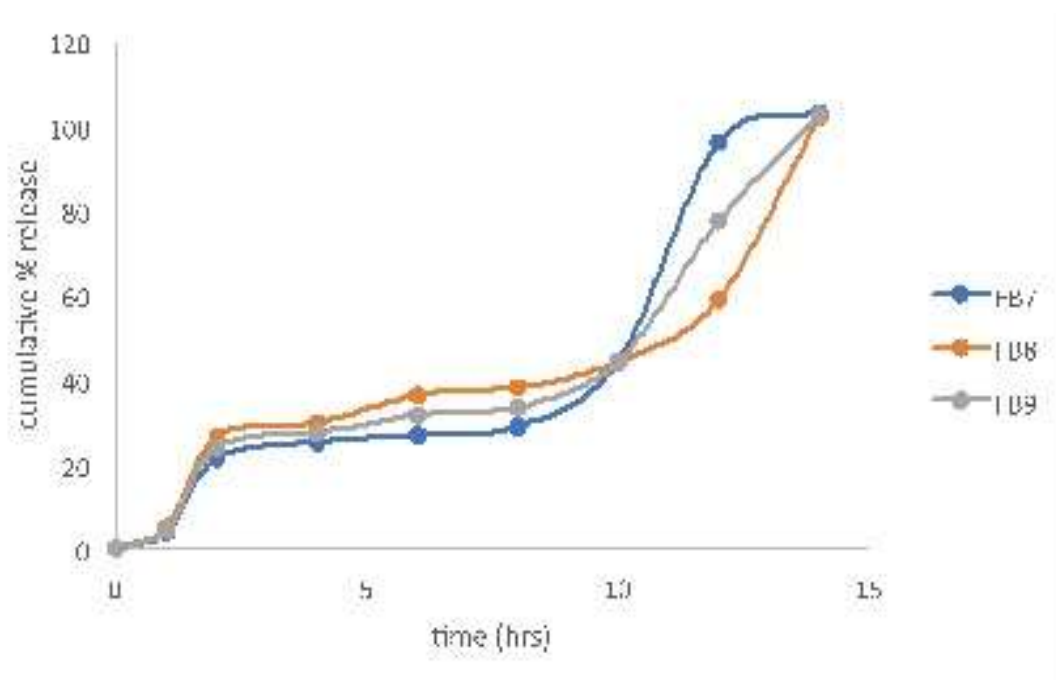


Figure 5. Graph Showing Cumulative % Drug Release Vs time for FB7, FB8, FB9.

6. CONCLUSION

Taken together, it is concluded that the swelling and floating sustained release Tablets of a model drug valacyclovir HCl were successfully formulated. The swelling and floating Tablets containing Sodium bicarbonate (12%) and SSG (10 %) (FB13) showed satisfactory results with respect to floating lag time, total floating duration, swelling ability, and sustained drug release properties. The optimized formulation FB13 followed zero-order kinetic model. Thus, ultimately, we formulated swelling and floating sustained release Tablets with an aim of increasing the MRT in the stomach with better and controlled delivery to the upper part of the small intestine where the drug has its absorption window. Thus, better absorption, improved bioavailability, local effect of drug, reduction in side effects, and also patient compliance of the product can improve the therapeutic efficacy of the medical treatment

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REFERENCES

1. Garg RG, Gupta GD. Progress in controlled gastroretentive delivery systems. Tropical journal of pharmaceutical research. 2008 Sep 11; 7(3):1055-66. <https://doi.org/10.4314/tjpr.v7i3.14691>
2. Kharia AA, Hiremath SN, Singhai AK, Omray LK, Jain SK. Design and optimization of floating drug delivery system of acyclovir. Indian journal of pharmaceutical sciences. 2010 Sep;72(5):599. <https://doi.org/10.4103%2F0250-474X.78527>
3. Bhavani A, Hemalatha B, Padmalatha K. Formulation development and in vitro Evaluation of sustained release matrix Tablets of Cefpodoxime proxetil. Asian Journal of Pharmacy and Technology. 2021;11(4):273-8. <http://dx.doi.org/10.52711/2231-5713.2021.00045>
4. Upadhyay P, Nayak K, Patel K, Patel J, Shah S, Deshpande J. Formulation development, optimization, and evaluation of sustained release Tablet of valacyclovir hydrochloride by combined approach of floating and swelling for better gastric retention. Drug delivery and translational research. 2014 Dec; 4:452-64. <https://doi.org/10.1007/s13346-014-0207-x>
5. Kalita BA, Saikia KR, Kalita BH. Formulation and evaluation of metronidazole microspheres-loaded bioadhesive vaginal gel. Asian J Pharm Clin Res. 2017;10(3):418-24. <http://dx.doi.org/10.22159/ajpcr.2017.v10i3.16417>
6. Patel S, Jain P, Parkhe G. Formulation and evaluation of acyclovir loaded novel nano-emulsion gel for topical treatment of herpes simplex viral infections. Journal of Drug Delivery and Therapeutics. 2018 Oct 1; 8(5-s):265-70 <https://doi.org/10.22270/jddt.v8i5-s.1968>
7. Sharma AR, Khan A. Gastroretentive drug delivery system: an approach to enhance gastric retention for prolonged drug release. International journal of pharmaceutical sciences and research. 2014 Apr 1; 5(4):1095. [http://dx.doi.org/10.13040/IJPSR.0975-8232.5\(4\).1095-06](http://dx.doi.org/10.13040/IJPSR.0975-8232.5(4).1095-06)
8. Karpe M, Mali N, Kadam V. Formulation development and evaluation of acyclovir orally disintegrating Tablets. Journal of Applied Pharmaceutical Science. 2012 Mar 30(Issue):101-5. <http://dx.doi.org/10.7324/JAPS.2012.2317>