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FORMULATION AND EVALUATION OF FLOATING TABLETS OF FAMCICLOVIR USING VARIOUS HYDROPHILIC AND HYDROPHOBIC POLYMERS

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Abstract:

Oral drug administration has been the predominant route for drug delivery. During the past two decades, numerous oral delivery systems have been developed to act as drug reservoirs from which the active substance can be released over a defined period of time at a predetermined and controlled rate. The present study is to develop Floating tablets of Famcyclovir. In this present study an attempt was made to increase the GI residence time of Famcyclovir, as the drug is having less gastric residence time, by formulating in to Floating tablets.

Systematic studies were conducted using different concentration of rate releasing polymer HPMC and Sodium carboxy methyl cellulosefor extending the drug release in upper GIT. All the prepared systems were evaluated for the different properties. Before the preparation of tablets, preformulation studies to find out the micromeritic properties to assess flowability, compressibility properties and solubility studies. And all the formulations gave good results for above preformulation studies.

Formulated tablets gave satisfactory results for various physical tablet evaluation parameters like tablet dimensions, hardness, friability, weight variation, buoyancy, content uniformity, all the formulations were found within the permissible range .Amongall the formulations (F1-F9), it was observed that formulation-1 has shown better buoyancy and dissolution profile. So Formulation-1 was found to be the best formulation among others.

*The kinetic treatment of the drug release data of the prepared formulations followed first order drug release; the prepared formulations followed HixonCrowel profile. It indicated that drug release was dissolution controlled and directly proportional to qube root of time. Hence **F1**was considered as formulation extending **99.85%** of drug was released at the end of 20 hrs. The stability studies were carried out for period of 3 months as per ICH guidelines and were in acceptable limits.*

Keywords: *Famcyclovir, hardness, friability, weight variation, buoyancy, content uniformity.*

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INTRODUCTION:

Over the past three decades, the pursuit and exploration of devices designed to be retained in the upper part of the gastrointestinal (GI) tract has advanced consistently in terms of technology and diversity, encompassing a variety of systems and devices such as floating systems, raft systems, expanding systems, swelling systems, bioadhesive systems and low-density systems [1]. Gastric retention will provide advantages such as the delivery of drugs with narrow absorption windows in the small intestinal region. Also, longer residence time in the stomach could be advantageous for local action in the upper part of the small intestine, for example treatment of peptic ulcer disease [2].

The retention of oral dosage forms in the upper GIT causes prolonged contact time of drug with the GI mucosa, leading to higher bioavailability, and hence therapeutic efficacy, reduced time intervals for drug administration, potentially reduced dose size and thus improved patient compliance [3]. Therefore, extended release DDS possessing gastric retention properties may be potentially useful [4].

Famciclovir is a guanosine analogue antiviral drug used for the treatment of various herpesvirus infections, most commonly for herpes zoster (shingles). Famciclovir is indicated for the treatment of herpes zoster (shingles), treatment of herpes simplex virus 2 (genital herpes), herpes labialis (cold sores) in immunocompetent patients and for the suppression of recurring episodes of herpes simplex virus. It is also indicated for treatment of recurrent episodes of herpes simplex in HIV patients [5].

The basic goal of therapy is to achieve a steady state blood level that is therapeutically effective and non-toxic for an extended period of time. The design of proper dosage regimens is an important element in accomplishing this goal.Floating tablets are drug delivery systems that are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of single dose in stomach region.The main aim is to Formulate and Evaluate Floating tablets of Famciclovir using various hydrophobic and hydrophobic polymers.

METHOD AND METHODOLOGY:

Colour, odor, taste and appearance:

The color, odor and taste of the drug were recorded using descriptive terminology.

Melting point determination [6]:

Melting point of the drug sample was determined by capillary method by using melting point apparatus. The reported and observed melting point is shown in Table.

Determination of solubility [7]:

The solubility of the Famcyclovir was determined by adding excess amount of drug in the solvent and equilibrium solubility was determined by taking supernatant and analyzing it on Lab India, double beam spectrophotometer.

% solubility = sample absorbance /standard absorbance × dilution factor ×100

Fourier Transformation Infra-red (FTIR) analysis [8]:

Infra-red spectroscopy analysis was performed by Fourier Transformation Infrared Spectrophotometer Alpha Brooker FTIR (Tokyo, Japan).The instrument was calibrated by using polystyrene film.

Ultraviolet Visible (UV-visible) spectroscopy [9]:

Construction of Calibration curve of model drugs by UV-Visible spectroscopy:

Preparation of Standard stock solutions:

Famcyclovir equivalent to 100 mg was weighed and transferred to 100 ml volumetric flask, dissolved in methanol and the final volume was made upto 100ml with 0.1N HCL. The resulted solution had the concentration of 1mg/ml (1000µg/ml) which was labeled as “stock solution A”.

From the stock solution A, 1 ml was pipette out in 10ml volumetric flask and the final volume was made upto 10ml with 0.1N HCL.The resulted solution had the concentration of 0.1mg/ml (100µg/ml) which was labeled as “stock solution B”. This stock solution B is used as working stock solution for further study. Further dilutions were prepared from the same solution.

Preparation of Standard solutions:

From the stock solution B, further dilution was made with 0.1N HCL in 10 ml volumetric flasks to get the solutions in the range of 2-10 µg/ml concentration and absorbance was recorded at 252 nm against suitable blank using UV-Spectrophotometer (UV-1601, Shimadzu, Japan).A calibration curve of absorbance against concentration was plotted and the drug follows the Beer’s & Lambert’s law in the concentration range of 2-10µg/ml. The Regression equation and correlation coefficient was determined.

Evaluation of Blend:

Angle of Repose [10]:

The flow property was determined by measuring the Angle of Repose. In order to determine the flow property, the Angle of Repose was determined. It is

the maximum angle that can be obtained between the free standing surface of a powder heap and the horizontal.

Angle of repose= $\tan^{-1}$ (h/r)

Where, h = height r = radius

Procedure:

- 20gms of the sample was taken
- The sample was passed through the funnel slowly to form a heap.
- The height of the powder heap formed was measured.
- The circumference formed was drawn with a pencil on the graph paper.

The radius was measured and the angle of repose was determined. This was repeated three times for a sample.

Bulk density [11]: Bulk density is ratio of given mass of powder and its bulk volume. Bulk density was determined by measuring the volume of known mass of powder sample that has been passed through the screen in to graduated cylinder or through volume measuring apparatus in to cup.

Bulk density = M / V_0

Where M= mass of the powder; V_0=bulk volume of the powder.

Tapped density:

A known quantity of powder was transferred to a graduated cylinder and volume V0 was noted. The cylinder fixed to a density determination apparatus, tapped for 200 times then reading was observed. The density is achieved by mechanically tapped by a measuring cylinder containing the powder sample. After observing the initial volume the cylinder is mechanically tapped and volume reading were taken until little further volume changes is observed.

Tap density = M / V_r

Where M = mass of the powder, V_r = final tapping volume of the powder.

Compressibility index and Hausner ratio [12]:

Basic methods for the determination of compressibility index and Hausner ratio:

While there are some variations in the method of determining the compressibility index and Hausner ratio, the basic procedure is to measure the unsettled apparent volume,(V_O), and the final tapped volume, (V_f), of the powder after tapping the material until no further volume changes occur. The compressibility index and the Hausner ratio are calculated as follows:

Compressibility index = 100 × Vo-V_f/Vo

Hausner ratio = Vo/V_f

Where, V_o = apparent volume, V_f= final tapped volume.

Alternatively, the compressibility index and hausner ratio may be calculated using measuredvalues of bulk density and tapped density as follows:

Compressibility index = 100 ×{ tapped density - bulk density / bulk density}

Hausner ratio = tapped density / bulk density

In a variation of these methods, the rate of consolidation is sometimes measured rather than, or in addition to, the change in volume that occurs on tapping. For the compressibility index and the hausner ratio, the generally accepted scale of flow ability is described in the following table.

Flow properties and corresponding Angle of repose, Compressibility index and Hausner ratio:

Table 1: Flow properties determination [13]

S. No	Flow properties	Angleof repose(θ)	Compressibility Index (%)	Hausner ratio
1	Excellent	25-30	<10	1.00-1.11
2	Good	31-35	11-15	1.12-1.18
3	Fair	36-40	16-20	1.19-1.25
4	Passable	41-45	21-25	1.26-1.34
5	Poor	46-55	26-31	1.35-1.45
6	Very poor	56-65	32-37	1.46-1.59
7	Very very poor	> 66	>38	>1.6

Evaluation of tablets:
The quantitative evaluation and assessment of a tablets chemical, physical and bioavailability properties are important in the design of tablets and to monitor product quality. There are various standards that have been set in the various pharmacopoeias regarding the quality of pharmaceutical tablets. These include the diameter, size, shape, thickness, weight, hardness, Friability, Buoyancy test and invitro-dissolution characters.

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

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

3. Weight variation test [14]:
This is an in process quality control test to ensure that the manufacturers control the variation in the weight of the compressed tablets, different pharmacopoeia specify these weight variation tests.. These tests are primarily based on the comparison of the weight of the individual tablets (xi) of a sample of tablets with an upper and lower percentage limit of the observed sample average (x-mean). The USP has provided limits for the average weight of uncoated compressed tablets. These are applicable when the tablet contains 50mg or more of the drug substance or when the latter comprises 50% or more, by weight of the dosage form.
Method:
Twenty tablets were weighed individually and the average weight was calculated. The individual tablet weights are then compared to the average weight. Not more than two tablets should differ in their average weight by more than percentages stated in USP. No tablet must differ by more than double the relevant percentage.
Table 2: Limits for Tablet Weight variation test:

Average weight of tablet (mg)	% Difference allowed
130 or less	10 %
From 130 to 324	7.5 %
> 324	5 %

4. Content Uniformity [15]:
The content uniformity test is used to ensure that every tablet contains the amount of drug substance intended with little variation among tablets within a batch. Due to increased awareness of physiological availability, the content uniformity test has been included in the monographs ofall coated and uncoated tablets and all capsules intended for oral administration where the range of size of the dosage form available include 50mg or smaller sizes.
Method:
Randomly select 30 tablets. 10 of these assayed individually. The Tablet pass the test if 9 of the 10 tablets must contain not less than 85% and not more than 115% of the labeled drug content and the 10th tablet may not contain less than 75% and more than 125% of the labeled content. If these conditions are not met, remaining 20 tablets assayed individually and none may fall outside of the 85 to 115% range.

Friability [16]:
Friction and shock are the forces that most often cause tablets to chip, cap or break. The friability test is closely related to tablet hardness and designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. It is usually measured by the use of the Roche friabilator.
Method:
A number of tablets are weighed and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed and the weight compared with the initial weight. The loss due to abrasion is a measure of the tablet friability. The value is expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked.
The percentage friability was determined by the formula:

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

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

Floating lag time [17]:
The time between the introductions of the tablet into the medium and its rise to upper one third
of the dissolution vesselis termed as floating lag time and the time for which the dosage form floats is term ed as the floating or flotation time. These tests are us ually performed in simulated gastric fluid or 0.1N

HCl maintained at 37 ^{0}C, by using USP dissolution a pparatus containing 900 ml of 0.1N HCl as the dissol ution medium.

Drug release [18]
The drug release from the Famcyclovir tablets was investigated in a USP-II (paddle) apparatus, 900 ml of 0.1N HCl(50 rpm, 37°C). At predetermined time intervals, 5-ml samples were withdrawn and take 1ml sample and diluted to 10 ml and then analyzed with UV spectrophotometry at λmax=256nm.

Drug release kinetics:
Dissolution data of above two methods was fitted in Zero order, First order and Higuchi equations. The mechanism of drug release was determined by using Higuchi equation.

Zero-Order Kinetics:
Zero order as cumulative amount of ***Percentage drug released v$_s$ time***

$$C = K_0 t$$

Where *K0* is the zero-order rate constant expressed in units of concentration/time and *t* is the time in hours. A graph of concentration vs time would yield a straight line with a slope equal to *K0* and intercept the origin of the axes.

First order kinetics:
First order as log cumulative percentage of ***log (%) cumulative drug remaining v$_s$time,***

$$Log C = Log C_o - k t / 2.303$$

Where $C_0$is the initial concentration of drug, *k* is the first order constant, and *t* is the time.

Higuchi Model:
Higuchi's model as ***cumulative percentage of drug released v$_s$ square root of time***

$$Q = K t_{1/2}$$

Where *K* is the constant reflecting the design variables of the system and *t* is the time in hours. Hence, drug release rate is proportional to the reciprocal of the square root of time.

KorsmayerPeppas equations:
Korsmeyerpeppas equation used to determine the mechanism of drug release form the polymer matrix of the tablet***. Log cumulative percentage of drug released VS Log time***, and the exponent *n* was calculated through the slope of the straight line.

$$M t / M_\infty = K t_n$$

Where *Mt/M_* is the fractional solute release, *t* is the release time, *K* is a kinetic constant characteristic of the drug/polymer system, and *n* is an exponent that characterizes the mechanism of release of tracers. For cylindrical matrix tablets, if the exponent $n = 0.45$, then the drug release mechanism is Fickian diffusion, and if $0.45 < n < 0.89$, then it is non-Fickian or anomalous diffusion. An exponent value of 0.89 is indicative of Case-II Transport or typical zero-order release.

Hixoncrowell erosion equation:
Hixson-Crowell cube root law, as the ***cube root of percentage drug remaining vs. time*** correlated the release from systems with polymer erosion/dissolution resulting in a change in surface area and diameter of particles or tablets.

$$Q_0^{1/3} - Q_t^{1/3} = kHC_t \ldots\ldots\ldots(4)$$

Where, Qt is the amount of drug released in time t, Q0 is the initial amount of the drug in the tablets, and kHC is the rate constant for the Hixson-Crowell rate equation.

Stability studies [19]:
Selected Formulation was subjected to stability studies as per ICH guidelines.
Following conditions were used for Stability Testing.
1. 25^{0}C/60% RH analyzed every month for period of three months.
2. 30^{0}C/75% RH analyzed every month for period of three months.
3. 40^{0}C/75% RH analyzed every month for period of three months.
The results are shown in Table
The optimized formulation F6 and Innovator sample are also kept for stability at room temperature for 3 months.

FORMULATION DEVELOPMENT

Procedures:

The Purpose of key ingredients included in the formulation.

Table 3: Composition of Acyclovir Floating Tablets

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Famcyclovir	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg
Chitosan	100 mg	200 mg	300 mg	---	---	33.3 mg	---	50 mg	50 mg
Carbopol 934	---	---	---	200 mg	---	33.3 mg	50 mg	---	50 mg
HPMC K15 M	---	---	---	---	200 mg	33.3 mg	50 mg	50 mg	---
Sodium bi carbonate	40 mg	40 mg	40 mg	40 mg	40 mg	40 mg	40 mg	40 mg	40 mg
Citric acid	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg
Micro Crystalline Cellulose	245 mg	145 mg	45 mg	145 mg	145 mg	245 mg	245 mg	245 mg	245 mg
Megnesium stearate	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg
Total Weight	600 mg	600 mg	600 mg	600 mg	600 mg	600 mg	600 mg	600 mg	600 mg

Procedure for Formulation:

Preparation of Formulation:

1. Drug and polymers pass through 40 # mesh separately and then transfer it to poly bag and mix it for 3 minutes.
2. Add diluents and other excipients to the above mixture. Finally add the Glidant (Magnesium Stearate) to the above blend mix it for 2min.
3. Compressed the above lubricated blend by using 10 mm round punches.

RESULTS AND DISCUSSION:

Evaluation of Preformulation parameters:

The properties like compressibility index, angle of repose and hausner ratio were calculated.

Table 4: Micromeritic properties of Active Pharmaceutical Ingredient:

S.No	Parameter	Results
1	Angle of repose	26.45± 0.1
2	Bulk Density	0.95±0.3 gm/ml
3	Tapped Density	1.02±0.2gm/ml
4	Compressibility Index	7.36±0.5%
5	Hausner's ratio	1.07±0.29

Conclusion: based on the above pre-formulation results it was observed that the flow is good.

Table 5: List of Micromeritic properties of directly compressible powder:

parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Angleof repose	$27^0 55'$	$29^o 39'$	23.31	$28^0 81'$	$28^0 65'$	$26^0 74'$	$28^o 39'$	$21^0 81'$	$24^0 81'$
Bulk density	0.63	0.55	0.51	0.47	0.60	0.57	0.46	0.42	0.61
Tapped density	0.66	0.63	0.54	0.52	0.64	0.63	0.51	0.53	0.69
%Compressibility	4.76	14.54	5.88	10.63	6.66	10.52	10.86	26.19	13.11
Hausner's ratio	1.047	1.14	1.05	1.10	1.06	1.10	1.10	1.15	1.13

Solubility Profile:

Solubility data of Famcyclovir

It is freely soluble in water, soluble in alcohols, and slightly soluble in common organic solvents, such as acetonitrile and methyl ethyl ketone.

D. Fourier Transformation Infra-red (FTIR) analysis:

Infra-red spectroscopy analysis was performed by Fourier Transformation Infrared Spectrophotometer Alpha Brooker FTIR (Tokyo, Japan).The instrument was calibrated by using polystyrene film.

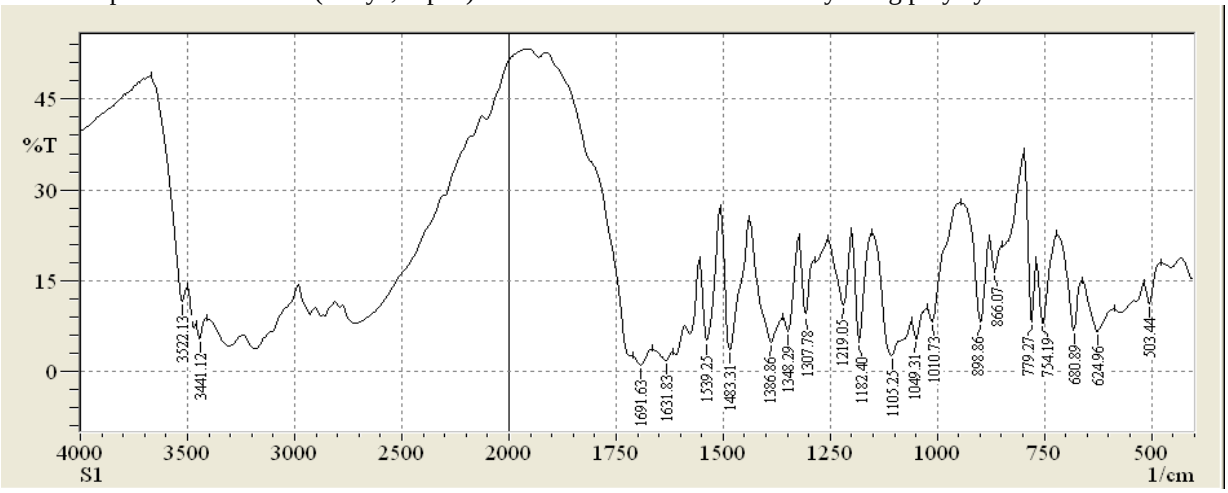


Fig.1: FT-IR Sample For Famcyclovir (Pure Drug)

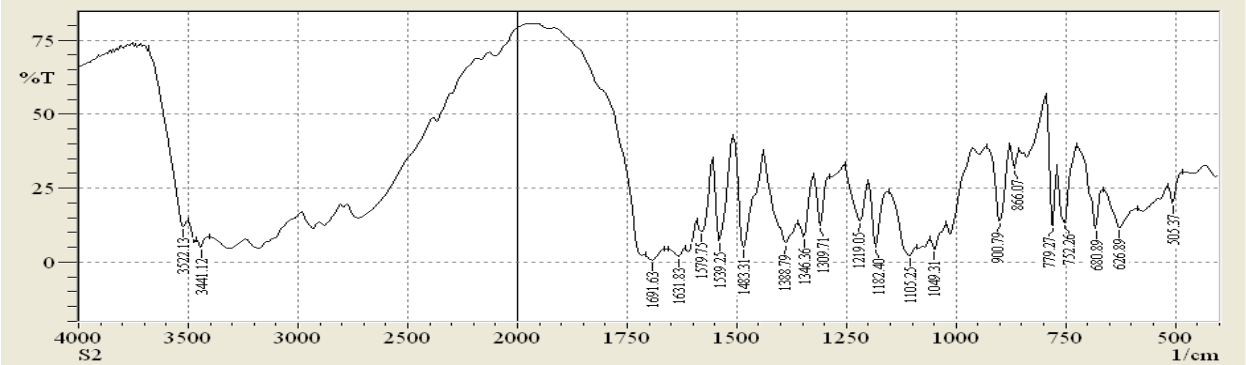


Fig.2: FT-IR Sample for Optimised Formulation F-1

Calibration of Standard Graph of Famcyclovir:

Construction of Calibration curve of model drugs by UV-Visible spectroscopy:

Preparation of Standard stock solutions:

Famcyclovir equivalent to 100 mg was weighed and transferred to 100 ml volumetric flask, dissolved in methanol and the final volume was made upto 100ml with 0.1N HCL. The resulted solution had the concentration of 1mg/ml (1000µg/ml) which was labeled as "stock solution A".

From the stock solution A, 1 ml was pipette out in 10ml volumetric flask and the final volume was made upto 10ml with 0.1N HCL.The resulted solution had the concentration of 0.1mg/ml (100µg/ml) which was labeled as "stock solution B". This stock solution B is used as working stock solution for further study. Further dilutions were prepared from the same solution.

Preparation of Standard solutions:

From the stock solution B, further dilution was made with 0.1N HCL in 10 ml volumetric flasks to get the solutions in the range of 2-10 µg/ml concentration and absorbance was recorded at 252 nm against suitable blank using UV-Spectrophotometer (UV-1601, Shimadzu, Japan).A calibration curve of absorbance against concentration was plotted and the drug follows the Beer's & Lambert's law in the concentration range of 2-10µg/ml. The Regression equation and correlation coefficient was determined.

Table 6: Standard graph of Famcyclovir in 0.1 N HCl at λ_{max}= 252nm

S. no.	CONCENTRATION(µg/ml)	ABSORBANCE
1	0	0
2	2	0.130
3	4	0.250
4	6	0.380
5	8	0.510
6	10	0.640

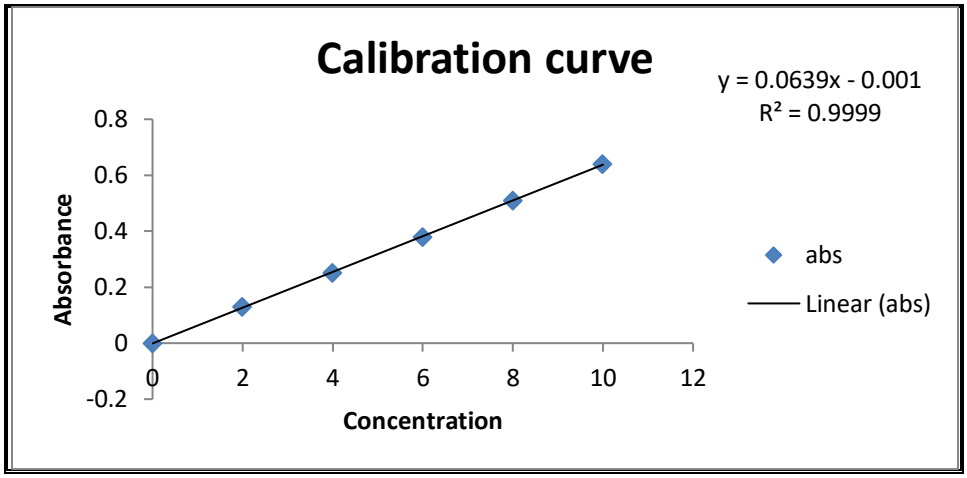


Fig.3: Standard graph of Famcyclovir:

Evaluation of the Prepared Tablets for Physical Parameters:

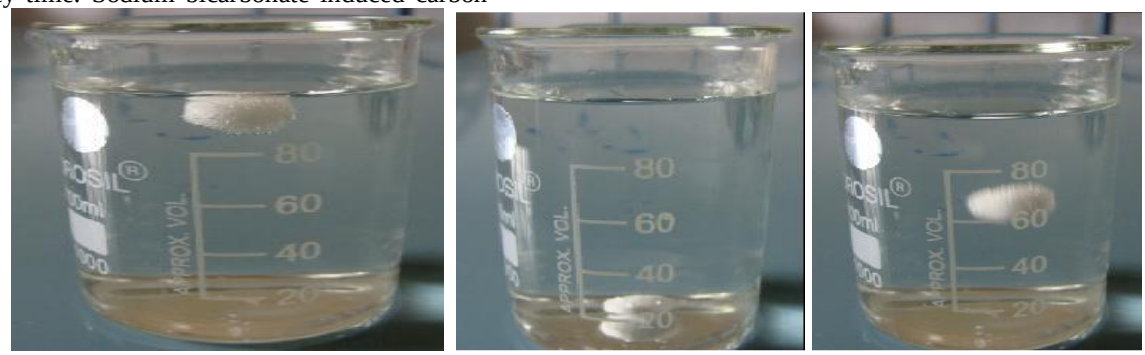
All formulations were tested for Physical parameters like Hardness, thickness, Weight Variation, Friability and found to be within the Pharmacopoeial limits. The results of the tests were tabulated. The drug content of all the formulations was determined and was found to be within the permissible limit. This study indicated that all the prepared formulations were good.

Table 7:Results for Evaluation parameters of all formulations

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Weight variation	0.600 ±0.004	0.599 ±0.005	0.5998 ±0.004	0.600 ±0.005	0.6 ±0.004	0.599 ±0.004	0.600 ±0.005	0.599 ±0.004	0.600 ±0.004
Thickness (mm)	5.5 ±0.4	5.6 ±0.4	5.3 ±0.4	5.6 ±0.4	5.5 ±0.4	5.5 ±0.3	5.5 ±0.4	5.5 ±0.1	5.5 ±0.2
Hardness (kg/cm^2)	8.9 ±1.4	7.4 ±1.2	8.2 ±1.2	6.9 ±0.9	8.4 ±1.9	8.1 ±1.7	8.2 ±1.5	8.3 ±1.6	8.2 ±1.4
Friability	0.22% ±0.2	0.26% ±0.23	0.25% ±0.19	0.25% ±0.26	0.25% ±0.22	0.22% ±0.1	0.21% ±0.4	0.21% ±0.5	0.21% ±0.7
Assay	99.91% ±0.2	99.84% ±0.4	99.87% ±0.3	98.88% ±0.2	99.88% ±0.3	99.89% ±0.2	99.88% ±0.2	99.68% ±0.2	99.88% ±0.2
Floating lag time (sec)	34	42	43	51	42	41	36	39	41

Floating lag time:

The floating tablets of Famcyclovir were prepared by using Chitosan, HPMC K15M, and Carbopol 934.Nine different formulations were prepared using different ratios of polymers. The prepared formulations were evaluated for floating lag time and buoyancy time. Sodium bicarbonate induced carbon dioxide generation in presence of dissolution medium (0.1 N HCl). It was observed that the gas generated is trapped and protected within the matrix, formed by polymers, thus density of the tablet decreased and it becomes buoyant.The floating lag time of the optimized formulation F-1 was 34 sec.



***In vitro* Dissolution studies:**

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

Apparatus : USP apparatus II (Paddle)
Agitation speed (rpm) : 50rpm
Medium : 0.1N HCl
Volume : 900 ml
Temperature : 37.0 ± 0.5 C
Time : 1, 4, 6, 8, 16, 20 hrs.
Wavelength : 252nm

The samples were withdrawn at predetermined time points, and were analyzed spectrophotometrically at 252nm.

Table 8: Results of Dissolution profile for F1-F9:

Time (Hrs)	%Drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	18.78	18.65	17.98	15.56	21.24	18.57	19.66	23.49	21.89
4	37.94	34.92	26.91	23.68	35.78	34.67	39.73	45.78	34.78
6	64.68	47.93	51.24	56.98	46.48	47.89	49.48	49.48	53.48
8	87.98	89.72	73.97	79.97	73.18	77.89	81.18	83.18	82.18
16	94.59	95.92	98.92	96.15	97.94	97.96	96.94	95.94	92.94
20	99.85	98.83	99.13	98.99	98.56	99.34	99.16	99.36	99.32

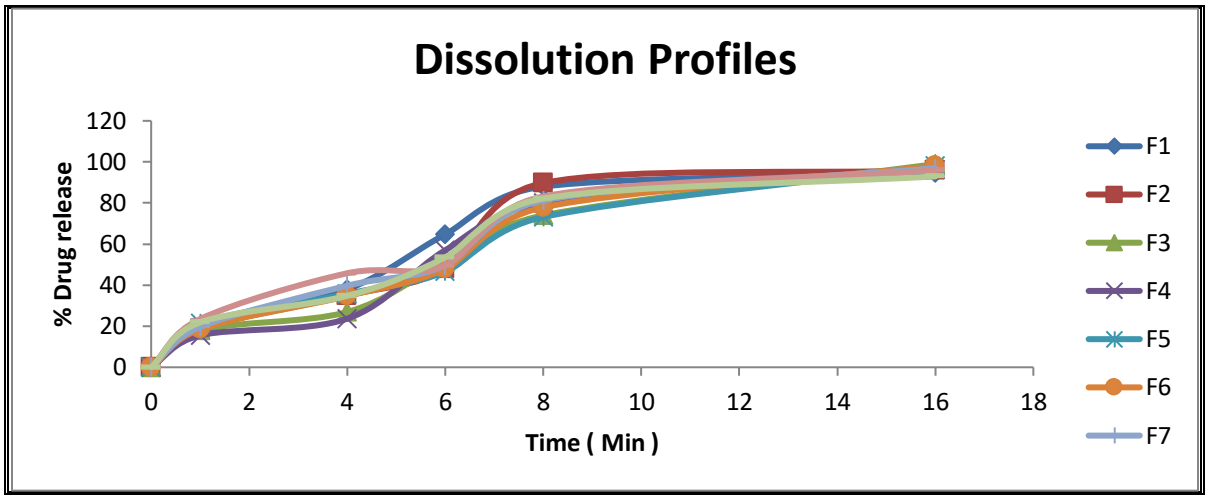


Fig.4: Dissolution study of F1-F7:

KINETIC MODELS:

Dissolution data of above two methods was fitted in Zero order, First order and Higuchi equations. The mechanism of drug release was determined by using Higuchi equation.

Table 9:Zero-Order Kinetics:

S.NO	TIME (Hrs)	%CR
1	**0**	0
2	**1**	18.78
3	**2**	37.94
4	**4**	64.68
5	**8**	87.98
6	**16**	94.59
7	**20**	99.85

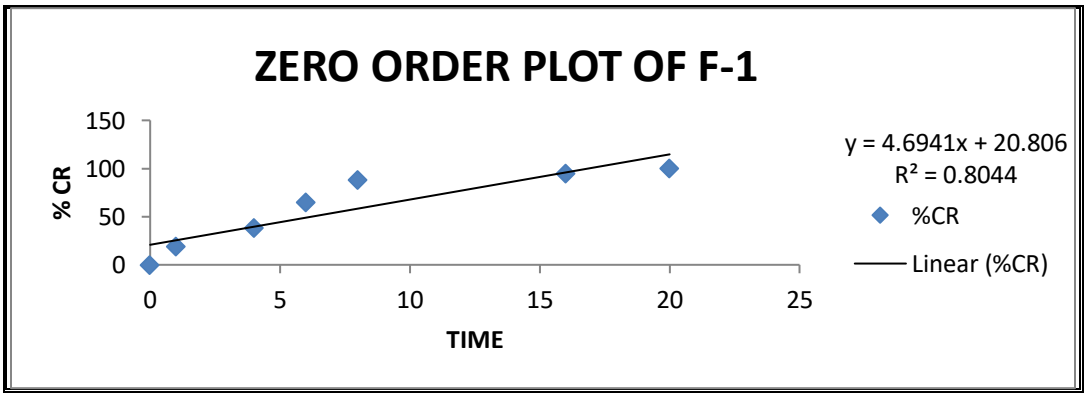


Fig.5: Zero Order Plot for Optimised Formulation

Table 10: First order kinetics:

S.NO	TIME (Hrs)	LOG% DRUG RETAINED
1	**0**	2
2	**1**	1.909663
3	**2**	1.792812
4	**4**	1.548021
5	**8**	1.079904
6	**16**	0.733197
7	**20**	-0.82391

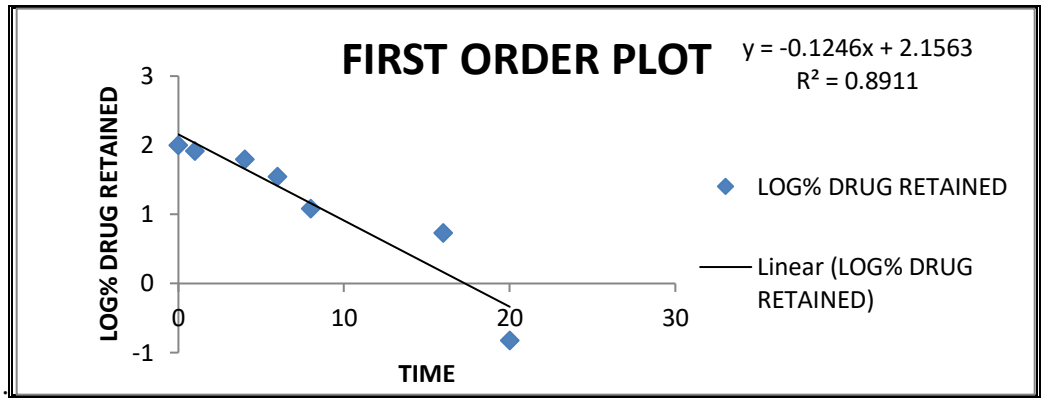


Fig.6: First Order Plot for Optimised Formulation

Table 11: Higuchi Model:

S.NO	Square root of Time	%CR
1	0	0
2	1	18.78
3	2	37.94
4	2.44949	64.68
5	2.828427	87.98
6	4	94.59
7	4.472136	99.85

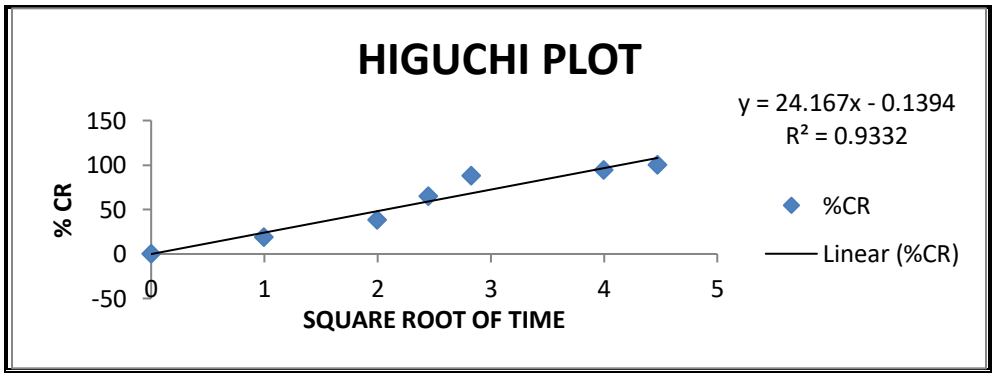


Fig.7: Higuchi Plot for Optimised Formulation

Table 12: KorsmayerPeppas equations:

S.NO	**log T**	**log %CR**
1	∞	0
2	0	1.273696
3	0.60206	1.579097
4	0.778151	1.81077
5	0.90309	1.944384
6	1.20412	1.975845
7	1.30103	1.999348

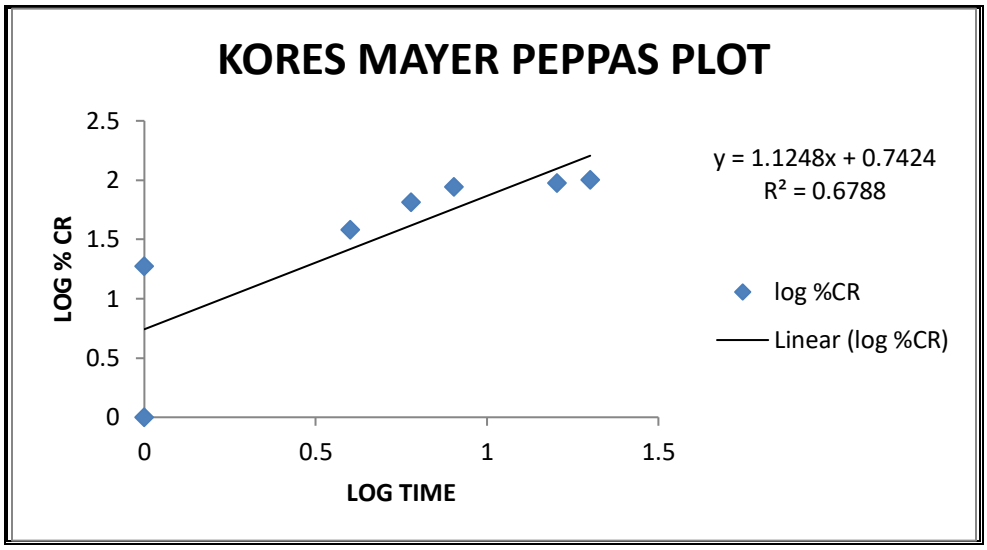


Fig.8: Kores Mayer Peppas Plot For Optimised Formulation

Table 13: Hixon Crowell erosion equation:

S.NO	TIME	CUBE ROOT OF %DRUG REMAINING
1	0	4.641
2	1	4.33
3	4	3.95
4	6	3.281
5	8	2.29
6	16	1.755
7	20	0.531

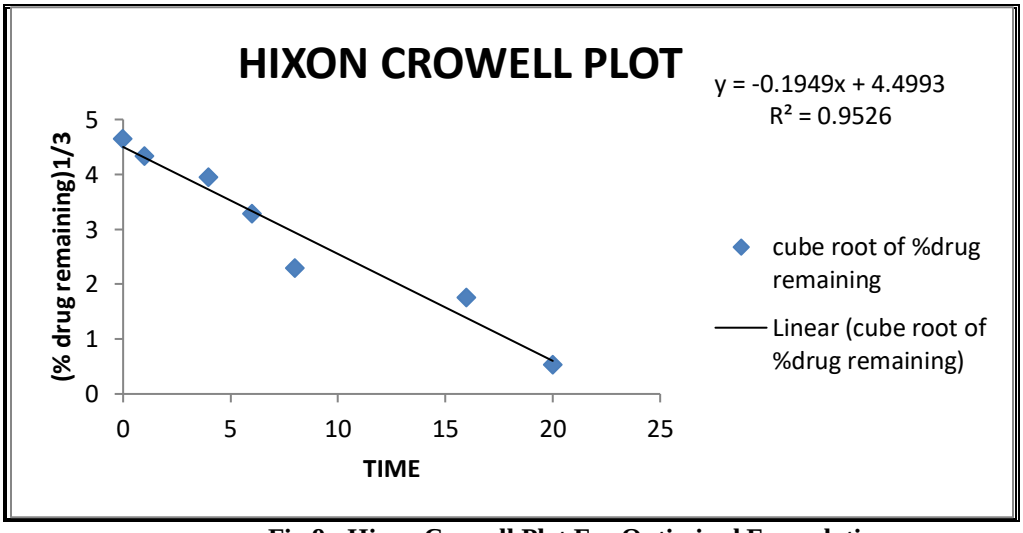


Fig.9: Hixon Crowell Plot For Optimised Formulation

Stability dissolution profile of F-1for 1st, 2nd & 3rd months

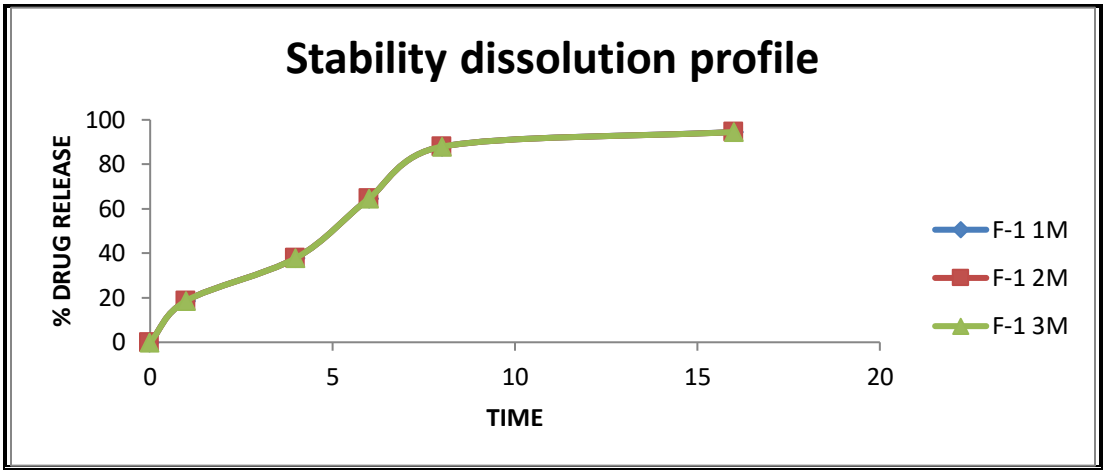


Fig.10: Stability dissolution profile of F-1for 1st, 2nd& 3rd months

CONCLUSION:

The objective of the present study is to develop Floating tablets of Famcyclovir. In this present study an attempt was made to increase the GI residence time of Famcyclovir, as the drug is having less gastric residence time, by formulating in to Floating tablets.

Systematic studies were conducted using different concentration of rate releasing polymer HPMC and Sodium carboxy methyl cellulosefor extending the drug release in upper GIT. All the prepared systems were evaluated for the different properties. Before the preparation of tablets, preformulation studies to find out the micromeritic properties to assess flowability, compressibility properties and solubility studies. And all the formulations gave good results for above preformulation studies.

Formulated tablets gave satisfactory results for various physical tablet evaluation parameters like tablet dimensions, hardness, friability, weight variation, buoyancy, content uniformity, all the formulations were found within the permissible range.

Finally it was concluded that:

Amongall the formulations (F1-F9), it was observed that formulation-1 has shown better buoyancy and dissolution profile. So Formulation-1 was found to be the best formulation among others.The kinetic treatment of the drug release data of the prepared formulations followed first order drug release; the prepared formulations followed HixonCrowel profile. It indicated that drug release was dissolution controlled and directly proportional to qube root of time. Hence ***F1***was considered as formulation extending **99.85%** of drug was released at the end of 20 hrs. The stability studies were carried out for period of 3 months as per ICH guidelines and were in acceptable limits.

REFERENCES:

1.. Fukuda M, Peppas NA, McGinity JW. Floating hot-melt extruded tablets for gastroretentive controlled drug release system. J Control Release. 2006;115(2):121–129.

2. Khan F, Ibn Razzak SM, Khan ZR, Azad MA, Chowdhury JA, Reza S. Theophylline loaded gastroretentive floating tablets based on hydrophilic polymers: preparation and *in vitro* evaluation. Pak J Pharm Sci. 2009;22(2):155–161.

3. Tamizharasi S, Rathi V, Rathi JC. Floating drug delivery system. Syst Rev Pharm. 2011;2(1):19–29.

4. Wanjari D. A review on floating drug delivery system. Int J Bioassays. 2014;3(8) 10.21746.

5. Wagstaff AJ, Faulds D, Goa K L. Acyclovir. A reappraisal of its antiviral activity, pharmacokinetic properties and therapeutic efficacy. Drugs. 1994; 47(1):153–205.

6. Tavakoli N, Varshosaz J, Dorkhoosh F, Motaghi S, Tamadon L. Development and evaluation of a monolithic floating drug delivery system for acyclovir. Chem Pharm Bull (Tokyo) 2012; 60(2):172–177.

7. Kharia AA, Hiremath SN, Singhai AK, Omray LK, Jain SK. Design and optimization of floating drug delivery system of acyclovir. Indian J Pharm Sci. 2010;72(5):599–606.

8. Trivedi P, Verma A, Garud N. Preparation and characterization of aceclofenac microspheres. Asian J pharm. 2008;2(2) DOI: 10.4103/0973-8398.42498.
9. Jain CP, Naruka PS. Formulation and evaluation of fast dissolving tablets of valsartan. Int J Pharm Pharm Sci. 2009; 1(1): 219–226.
10. United States Pharmacopoeia. 26th ed. Springer: Twin Brook Park Wag, United States; pp. 1323–1607.
11. Vinay W, Yallagatti MS, Varma MM. Formulation, development and evaluation of novel floating tablet of metoclopramide hydrochloride. J Pharm Res. 2011;4(10):3678.
12. Dorozynski P, Jachowicz R, Kulinowski P, Kwiecinski S, Szybinski K, Skorka T, et al. The macromolecular polymers for the preparation of hydrodynamically balanced systems--methods of evaluation. Drug Dev Ind Pharm. 2004; 30(9): 947–957.
13. Basak SC, Rahman J, Ramalingam M. Design and *in vitro* testing of a floatable gastroretentive tablet of metformin hydrochloride. Pharmazie. 2007; 62(2):145–148.
14. Emami J. *In vitro-in vivo* correlation: from theory to applications. J Pharm Pharm Sci. 2006; 9(2):169–189.
15. Chatzizaharia KA, Hatziavramidis DT. Dissolution efficiency and design space for an oral pharmaceutical product in tablet form. IndEngChem Res. 2015; 54(24): 6305–6310.
16. Dash S, Murthy PN, Nath L, Chowdhury P. Kinetic modeling on drug release from controlled drug delivery systems. Acta Pol Pharm. 2010; 67(3): 217–223.
17. Emami J J, Bazargan N N, Ajami A. HPLC determination of acyclovir in human serum and its application in bioavalibility studies. 2009;4(1):47–54.
18. Jiménez-Martínez I, Quirino-Barreda T, Villafuerte-Robles L. Sustained delivery of captopril from floating matrix tablets. Int J Pharm. 2008; 362(1-2): 37–43.
19. Javadzadeh Y, Hamedeyazdan S, Adibkia K, Kiafar F, Zarrintan MH, Barzegar-Jalali M. Evaluation of drug release kinetics and physico-chemical characteristics of metronidazole floating beads based on calcium silicate and gas-forming agents. Pharm characteristics of metronidazole floating beads based on calcium silicate and gas-forming agents. Pharm Dev Technol. 2010; 15(4): 329–338.