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Formulation Optimization and *In-Vitro* Evaluation of Floating Tablet of Stavudine.

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ABSTRACT

Different formulation technologies intended for gastro retentive dosage form were investigated and patented over the years. The aim of this study was to formulate, optimize and evaluate the gastro retentive floating tablet of stavudine. The developed technology induces a low density dosage form containing high concentration of active pharmaceutical ingredient (API). In the present work, the in-vitro sustained release of stavudine from matrix of tablet containing HPMC K100M and Xanthan gum as release retardant polymers has been studied. Sodium bi-carbonate and citric acid are used as gas generating agents. The tablets were prepared by direct compression method. The tablets eroded upon contact with the release medium 0.1N HCl and the relative importance of floating lag time,% swelling index and % drug release patterns varied significantly with the concentration of polymers. Optimization was done by using design expert 8.0.4.1 and optimized formulation F6 of stavudine floating tablet shows no significant change in hardness, drug content, floating lag time and % cumulative drug release pattern after the stability period of 3 months at 40^0c/75% relative humidity.

Key-words- Stavudine, HPMC, Xanthan gum, floating tablet, in vitro buoyancy.

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INTRODUCTION

Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulation etc. From immediate release to site specific delivery, oral dosage forms have really progressed. Gastroretentive dosage forms significantly extend the period of time, over which drug may be released and thus prolong dosing intervals and increase patient compliance. Such retention systems are important for those drug that are degraded in the intestine like antacids or certain antibiotics, enzymes that act locally in the stomach. This systems can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the gastrointestinal tract, thus ensuring optimal bioavailability. Various gastroretentive techniques were used, including floating, swelling, high density, and bioadhesive system, have been explored to increase the gastroretention of dosage forms .

MATERIALS AND METHODS

Materials-

Stavudine was obtained from CIPLA Ltd., (Mumbai, India). HPMC K100M and Xanthan gum were received as gift samples from Concept Pharma Pvt. Ltd., (Aurangabad, India).Other materials such as sodium bi-carbonate, citric acid, Talc, Mannitol and Magnesium Stearate were purchased from modern laboratories, (Nashik, India).

Table 1: Composition of Stavudine floating tablet.

Ingredients *	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Stavudine	110	110	110	110	110	110	110	110	110
HPMC K100M	30	60	90	30	60	90	30	60	90
Xanthan gum	15	22.5	30	22.5	30	15	30	15	22.5
Sodium bicarbonate	60	60	60	60	60	60	60	60	60
Citric Acid	12	12	12	12	12	12	12	12	12
Talc	9	9	9	9	9	9	9	9	9
Magnesium Stearate	3	3	3	3	3	3	3	3	3
Mannitol	81	43.5	6	73.5	36	21	66	51	13.5
Total	**320**	**320**	**320**	**320**	**320**	**320**	**320**	**320**	**320**

Preparation of floating tablets: [1]

The composition of different formulations of stavudine floating tablets is shown in Table 1. Different tablet formulations were prepared by direct compression technique. All the powders passed through 40/60 mesh sieve. The required quantity of drug, various polymers and other ingredients were mixed thoroughly. Talc and magnesium stearate were finally added as a glidant and lubricant respectively. The blend was directly compressed (10mm diameter, round flat faced

punches) using multiple punch tablet compression machine (General Machinery Co, Mumbai., India). Each tablet contained 110 mg of stavudine.

Characterization of powder blend: [1,2,3]

The tablet blend were evaluated for their bulk density, tapped density, compressibility index, angle of repose and Hausner ratio. The tapping method was used to determine the bulk density, tapped density, percent compressibility index and Hausner ratio.

$$\text{Compressibility index} = *\rho t\text{-}\rho b / \rho t] \times 100$$

$$\text{Hausner ratio} = \rho t / \rho b$$

Where ρt = tapped density

ρb = initial bulk density of tablet blend.

Angle of repose θ of the tablet blend measures the resistance to particle flow and was determined by fixed funnel method.

Differential scanning calorimetry (DSC): [4, 5, 6]

The DSC analysis of pure drug, drug+ HPMC K100M+Xanthan gum were carried out using a Shimadzu DSC 60, (Japan) to evaluate any possible drug-polymer interaction. The 2 mg sample were heated in a hermetically sealed aluminum pans in the temperature range of 25-30ºc at heating rate of 10ºc /min under nitrogen flow of 30ml/min.

Evaluation of floating tablets:

The prepared floating tablets were evaluated for Dimension (Diameter and Thickness) using 6 tablets (vernier calipers), uniformity of weight using 20 tablets (analytical balance Contech CA224), hardness using 6 tablets (Monsanto hardness tester), friability using 20 tablets (Kumar Mfg. Ltd. Roche type friabilator).

Drug content uniformity-[7]

The tablets (n=3) were randomly selected from each batch of formulation and subjected for content uniformity test. The tablets were taken and milled separately by using Glass mortar and pestle then powder equivalent to 10 mg of drug were accurately weighed and transfer 50ml of 0.1N Hcl solution and stirr to mix properly. Resulting solution was filter through whatmman filter paper and the final volume adjusted with 0.1N Hcl up to 100ml. Then the suitable dilutions were prepared and samples were analyzed by using validated uv visible spectrophotometer (Shimadzu-2450 UV-VISIBLE spectrophotometer) at 266 nm using 0.1N Hcl as blank.

In-vitro buoyancy-[8,9]

The In-Vitro buoyancy was characterized by floating lag time and total floating time. As per the method described by Rosa et al, the tablets were placed in a 100 ml beaker containing 0.1N HCl,

which was maintained at 37°C. The time required for the tablet to rise to the surface of the medium was determined as the buoyancy lag time or floating lag time. The duration of which the dosage form constantly remained on the surface of medium was determined as the total buoyancy time or total floating time.

Swelling Index - [10]

The swelling studies of the tablets were determined in at room temperature. The swelling study of the tablet was done using USP II dissolution apparatus. The medium used was 0.1N HCl, 900 ml, rotated at 100 rpm. The medium was maintained at 37 ± 0.5^0C throughout the study. At every 1 hr, the tablets were withdrawn, blotted to remove excess water, and weighed. After draining free water by blotting with tissue paper, these were weighed for weight gain on the analytical balance. Swelling index (SI) was calculated by using the following formula;

$$\mathbf{SI} = \frac{\mathbf{weight\ of\ tablet\ at\ time\ t - weight\ of\ tablet\ before\ immersion}}{\mathbf{weight\ of\ tablet\ before\ immersion}}$$

In-Vitro Dissolution Studies-[8,11,12,13]

The release rate of Stavudine from floating tablets was determined using USP Dissolution Testing Apparatus type-II (LABINDIA-DISSO TEST 6 F 622). The dissolution test was performed using 900 ml of 0.1N HCl, at 37 ± 0.5°C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus hourly and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µ membrane filter and diluted to a suitable concentration with 0.1N HCl. Absorbance of these solutions was measured at 266 nm using a Shimadzu-2450 UV-VISIBLE spectrophotometer. For each formulation, the experiments were carried out in triplicate. The release data were calculated by using PCP disso V3 software.

Optimization of floating tablet-[14,15]

Optimization study was performed using Design Expert® software (Design Expert trial version 8.0.1; State-Ease Inc., Minneapolis, MN, USA). A general factorial design was used for systemic study of combination polymer HPMC K 100 M and Xanthan gum. A general factorial design was constructed where the amounts of HPMC K100 M (X1) and Xanthan gum (X2) was selected as the independent variables i.e. factors. The levels of these factors were selected on the basis of initial studies and observations. All the other formulation aspects and processing variables were kept invariant throughout the study period.

Stability study:[16,17,18]

Stomach specific tablets of stavudine formulated and accelerated stability studies were carried out as per ICH guidelines. The prepared stavudine floating tablets containing HPMC K100M

(F5) were selected for stability study on the basis of in vitro buoyancy and in vitro drug dissolution studies. The floating tablets were stored at 40°C/75% RH in closed high density polyethylene bottles for 3 months. The samples were withdrawn after periods of 1 month, 2 month and 3 month. The samples were analyzed for its hardness, floating characteristics, drug content and In vitro drug release.

RESULT AND DISCUSSION

The prepared floating tablets were evaluated for thickness, weight variation, hardness, friability, drug content, swelling index, in vitro buoyancy studies, in vitro drug dissolution studies and stability studies. All the studies were performed in triplicate, and results are expressed as mean ± SD.

Characterization of powder blend-

The powders prepared for compression of floating tablets were evaluated for their flow properties, the results were shown in Table 2. Angle of repose was in the range of 20.29 to 22.11^0 which indicates excellent flow of the powder for all formulations. The bulk density of the powder formulation was in the range of 0.732 to 0.745 gm/ml; the tapped density was in the range of 0.820 to 0.842 gm/ml, which indicates that the powder was not bulky. The carr's index for all the formulations was found to be below 15% indicating that the powders have a Good compressibility. The hausner ratio for all the formulations was found to be <1.25, indicating good flow properties. These values indicate that the prepared granules exhibited good flow properties.

Table 2: Table shows flow properties of powder

Formulation Code	Loose bulk density (gm/cm3)	Tapped bulk density (gm/cm3)	Hausner ratio (HR)	Carr's index (CI)	Angle of repose (θ°)
F1	0.745	0.842	1.13	11.52	21.17
F2	0.732	0.820	1.122	10.73	21.19
F3	0.743	0.820	1.10	9.39	20.54
F4	0.743	0.820	1.10	9.39	22.11
F5	0.732	0.842	1.01	13.22	20.82
F6	0.732	0.842	1.15	13.06	20.29
F7	0.743	0.820	1.10	9.39	21.39
F8	0.743	0.820	1.10	9.39	20.59
F9	0.743	0.842	1.13	11.75	20.76

Differential scanning calorimetry (DSC)

Any possible drug polymer interaction can be studied by thermal analysis. Stavudine exhibits a sharp endothermic peak at 174.21 °C shown in figure 1(a), which corresponds to its melting

point. The stavudine + HPMC K100M + Xanthan gum exhibit a sharp endothermic peak at 174.77ºC shown in figure 1(b), Hence DSC study shows that there is no any drug polymer interaction.

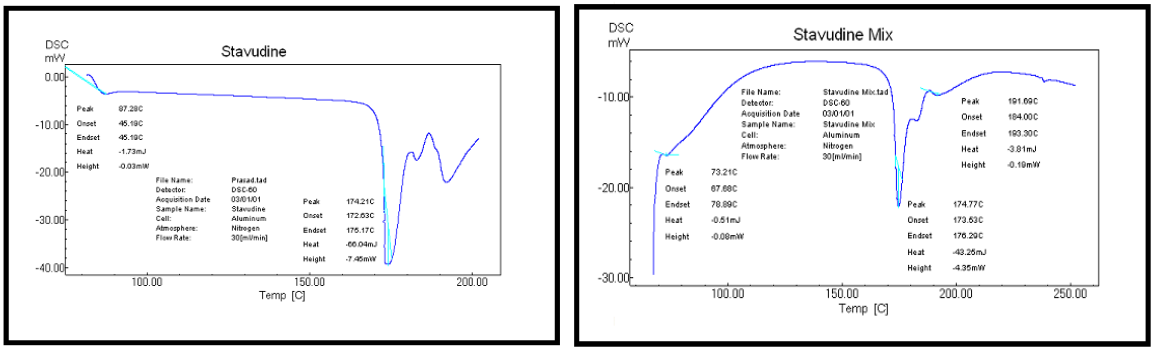

Figure 1 (a): DSC thermogram of Stavudine. (b): DSC thermogram of mixture

Physicochemical evaluation of floating tablets-

The floating stavudine tablets were off-white, smooth, and flat shaped in appearance. The results of physicochemical characterizations are shown in Table 3.

Table 3: Physicochemical characterization of Stavudine floating tablets

Code	Dimension		Hardness (kg/cm^2)**	Friability (%)***	Weight variation(%)****	Drug content (%w/w)***
	Diameter	Thickness				
F1	10.07±0.0	4.04±0.00	5.8±0.25	0.70	318.8±3.62	96.9±0.05
F2	10.07±0.0	4.04±0.00	5.7±0.27	0.61	319.5±2.76	94.05±2.80
F3	10.07±0.0	4.05±0.00	5.5±0.44	0.69	317.5±3.52	97.42±0.12
F4	10.07±0.0	4.07±0.01	5.6±0.41	0.75	319.4±3.34	97.42±0.12
F5	10.07±0.0	4.05±0.02	5.7±0.27	0.69	318.8±3.54	95.10±3.75
F6	10.07±0.0	4.05±0.01	5.58±0.62	0.70	317.6±4.12	96.30±0.10
F7	10.07±0.0	4.06±0.01	5.58±0.37	0.72	316.3±4.77	97.62±1.22
F8	10.07±0.0	4.06±0.01	5.5±0.44	0.73	317.5±3.34	96.85±0.22
F9	10.07±0.0	4.04±0.01	5.66±0.32	0.69	318.4±4.52	97.85±1.00

All the values are expressed as mean± S.D., *n=10, ** n=3 and *** nC2, ****=20

The thickness of floating tablets was measured by vernier caliper and was ranged between 4.04±0.10 and 4.07±0.11 mm. The weight variation for different formulations (F1 to F9) was found to be 316.3±4.77% to 319.5±2.76%, showing satisfactory results as per Indian Pharmacopoeia (USP) limit. The hardness of the floating tablets was measured by Monsanto tester and was controlled between 5.5±0.44 and 5.8±0.25 kg/cm2. The friability was below 1% for all the formulations, which is an indication of good mechanical resistance of the tablet. The percentage of drug content for F1 to F9 was found to be in between 94.05±2.80 to 97.85±1.0 of stavudine, it complies with official specifications.

Floating characteristic

All the batches of tablets were found to exhibit short floating lag times due to presence of sodium bicarbonate and citric acid. The tablets with high concentrations of HPMC K100 M (90 mg) and low concentration of Xanthan gum (15 mg) exhibited short floating lag time (72 seconds) and floated for longer duration (24Hrs). This indicated that the molecular weight distribution or viscosity of the gel-forming polymer HPMC K100 M and Xanthan gum influences the in-vitro buoyancy and total floating time.

All the prepared tablets shows the total floating time more than 24 hours except the F1 batch shows only more than 12 hours. From the results it can be concluded that the concentration of polymer increased, decrease the floating lag time and increase the total floating time.

Table 4: Data of In-Vitro buoyancy study.

Formulation code	Floating lag time (Sec)*	Total floating time (hrs)*
F1	91±1.73	>12
F2	82±2.08	>24
F3	87±2.64	>24
F4	79±1.52	>24
F5	79±1.52	>24
F6	72±1.15	>24
F7	75±0.57	>24
F8	89±2.08	>24
F9	82±1.00	>24

Swelling Index

Swelling study was performed on all the batches (F1 to F9) for 12 hours. The result of swelling index were shown in figure 2, it shows the plot of swelling index as a function of time for different formulation. It was observed that the swelling indices were increased with increase in polymer concentration. Swelling was strong enough to avoid premature disintegration as well as burst effect and retarded the release of pure drug for a long period of time. Complete swelling was achieved by the end of seven to nine hours for different formulation. Swelling index values starts decreasing when polymer erosion starts in medium. The result of swelling index for optimized formulation F6 were shown in table 5.

Table 5: swelling index and % drug release data of optimized formulation F6

Time(Hrs)	Swelling Index (%)	% Drug Release
0	0	0
2	1.91±0.020	13.28±0.68
4	2.24±0.010	35.21±0.28
6	2.39±0.015	61.41±0.24
8	2.52±0.015	77.51±0.41
10	2.71±0.015	87.47±0.52
12	3.07±0.015	98.08±0.33

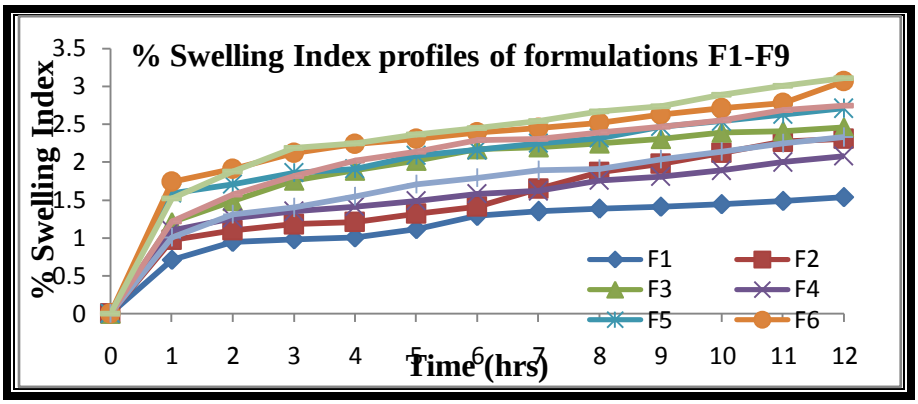

Figure 2: % Swelling profile of formulations F1-F9

In-Vitro Dissolution Studies

In-vitro dissolution studies of all the formulations of floating tablets of Stavudine were carried out in 0.1 N HCl. The study was performed for 12 hours, and percentage drug release was calculated at 2 hours time intervals. The results of in vitro dissolution studies of all formulations were shown in Figure 3. The variation in drug release was due to different types of polymers and different concentrations of polymer in all the nine formulations. Formulation F6 meets the needed theoretical drug release profile and floated with a lag time of 72 ±1.15 seconds. Formulation F1 shows about 99.62% of cumulative drug release up to 8 hrs. This formulation shows very fast drug release profile than all other formulations. This may be due to low concentration of HPMC K100 and Xanthan gum than all other formulations. Formulation F4 shows about 99.08% of % cumulative drug release profile up to 10 hrs. Formulations F7 and F8 shows above 90% of % cumulative drug release profile up to 11 hrs and all other formulations (F2, F3, F5, F6 and F9) shows 80 – 98.08 % release of drug up to 12 hrs.

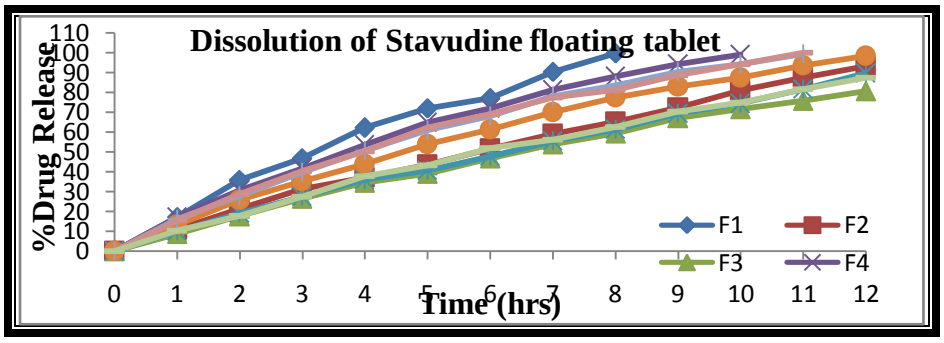

Figure 3: Dissolution profiles of formulations F1-F9.

From the above study it was concluded that the formulation F6 showed the sustained drug release profile with good matrix integrity, less floating lag time with good total floating time and good swelling index profile as compared with the selected batches. Formulation F5 shows highest regression coefficient ($\mathbf{R^2}$) value (0.9992) than all other formulations. Thus from the

above results **formulation F6** was concluded as the optimum formulation among all the nine formulations of this series. Hence the formulation F6 was selected for further stability study.

and according to results of optimization, it was considered that the formulation F6 was best formulation among all the nine formulations of this series. The percentage drug release data of formulation F6 were shown in table 5.

Kinetic modeling of drug release

The data obtained from in vitro dissolution studies were fitted in different models viz. zero order, first order, Higuchi and Korsemeyer- Peppas equation, the results were shown in Table **6**.

Table 6: Different kinetic models for Stavudine floating tablets (F1 to F9)

Formulations	Zero order	First order	Higuchi	K-Peppas		Best fit model
	R^2	R^2	R^2	R^2	n	
F1	0.9823	0.8015	0.8015	0.9949	0.8241	K-Peppas
F2	0.9929	0.9367	0.9367	0.9787	0.8416	K-Peppas
F3	0.9905	0.9868	0.9868	0.9982	0.8814	K-Peppas
F4	0.9733	0.8900	0.8900	0.9982	0.7697	K-Peppas
F5	0.9947	0.9492	0.9492	0.9978	0.8620	K-Peppas
F6	0.9769	0.9061	0.9061	0.9992	0.7989	K-Peppas
F7	0.9700	0.8564	0.8564	0.9977	0.7686	K-Peppas
F8	0.9672	0.7927	0.7927	0.9966	0.7690	K-Peppas
F9	0.9903	0.9708	0.9708	0.9979	0.8658	K-Peppas

Optimization of the formulation and data analysis.

For matrix tablets, an n value near to 0.5 indicates diffusion control and an n value near to 1 indicates relaxation or erosion control. The intermediate value suggests that diffusion and erosion contributes to overall release mechanism. A value of n for all matrices studied here was ranged between 0.7686 to 0.8814 which indicating an anomalous behavior corresponding to swelling, diffusion and erosion mechanism. Thus drug release was found to be controlled by diffusion and matrix erosion mechanism. All formulations shows $\mathbf{R^2}$ values in range of 0.9787-0.9992. Among all formulations formulation F6 shows highest $\mathbf{R^2}$ value (0.9992). Thus this formulation was concluded to be optimum formulation among 9 formulation batches.

Design Summary.

The design used for the optimization is the 3- level factorial design with linear design model based on the response surface methodology. There were two factors which affect the Floating lag time, % Swelling Index, % Cumulative drug release. Viz. Factor A.HPMC K 100 M, and B. Xanthan gum.

Table 7: Design summary

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Study Type	Response Surface		**Runs**	9								
Design Type	Optimal	Best	**Blocks**	No Blocks								
Design Model	3 Level Factorial		**Build Time (ms)**	19.05								
Factor	**Name**	**Units**	**Type**	**Sub type**	**Minimum**	**Maximum**	**-1 Actual**	**+1 Actual**	**Mean**	**SD.**		
A	HPMC k 100	Mg	Numeric	Continuous	30	90	30	90	60	24.49		
B	Xanthan Gum	Mg	Numeric	Continuous	15	30	15	30	22.5	6.12		
Response	**Name**	**Units**	**Obs**	**Analysis**	**Minimum**	**Maximum**	**Mean**	**Std. Dev.**	**Ratio**	**Trans**	**Model**	
Y1	% Drug Release	%	9	Polynomial	80.77	99.83	94.22	6.87	1.33	None	Linear	
Y2	Swelling Index	%	9	Polynomial	1.54	3.11	2.46	0.46	2.01	None	Linear	
Y3	Floating lag time	Sec	9	Polynomial	68	91	81.33	7.19	1.23	None	Linear	

Analysis of Variance (ANOVA).

Table 8: ANOVA result for Floating Lag Time.

Source	Sum Of Squares	df	Mean Square	F Value	P-value Prob > F	
Model Significant	325.08	3	108.36	6.09	0.0401	Signifacant
A- HPMC K 100 M	10.67	1	10.67	0.60	0.4737	
B-Xanthan gum	8.17	1	8.17	0.46	0.5281	
AB	306.25	1	306.25	17.22	0.0089	
Residual	88.92	5	17.78	-	-	
Cor Total	414	8	-	-	-	

- The Model F-value of 6.09 implies the model is significant.
- There is only a 4.01% chance that a "Model F-Value" this large could occur due to noise.
- Values of "Prob > F" less than 0.0500 indicate model terms are significant.In this case A are significant model terms.
- Values greater than 0.1000 indicate the model terms are not significant.

Table 9: ANOVA result for Swelling Index.

Source	Sum Of Squares	df	Mean Square	F Value	P-value Prob > F	
Model Significant	1.34	3	0.45	5.77	0.0444	Significant
A- HPMC K 100 M	0.98	1	0.98	12.75	0.0160	
B-Xanthan gum	0.027	1	0.027	0.35	0.5822	
AB	0.32	1	0.32	4.21	0.0954	
Residual	0.39	5	0.077	-	-	
Cor Total	1.72	8	-	-	-	

- The Model F-value of 5.77 implies the model is significant.
- There is only a 4.44% chance that a "Model F-Value" this large could occur due to noise.
- Values of "Prob > F" less than 0.0500 indicate model terms are significant.In this case A are significant model terms.
- Values greater than 0.1000 indicate the model terms are not significant.

Table 10: ANOVA result for % Cumulative drug Release.

Source	Sum Of Squares	Df	Mean Square	F Value	P-value Prob > F	
Model Significant	367.83	3	122.61	143.98	< 0.0001	Significant
A- HPMC K 100 M	160.99	1	160.99	189.05	< 0.0001	
B-Xanthan gum	130.01	1	130.01	152.67	< 0.0001	
AB	76.83	1	76.83	90.21	0.0002	
Residual	4.26	5	0.85			
Cor Total	372.09	8				

- The Model F-value of 143.98 implies the model is significant.
- There is only a 0.01% chance that a "Model F-Value" this large could occur due to noise.
- Values of "Prob > F" less than 0.0500 indicate model terms are significant.In this case A,B.AB are significant model terms.
- Values greater than 0.1000 indicate the model terms are not significant.

Model Assessment of linear term.

A. Model for Floating lag time.

After putting the data in Design Expert Software, fit summary applied to data in that linear model had been suggested by software. Floating lag time follows linear model.

Floating lag time = **+140 - 0.91944 HPMC K100M - 2.4888 Xanthan gum**

+ 0.03888 HPMC K100M * Xanthan gum.

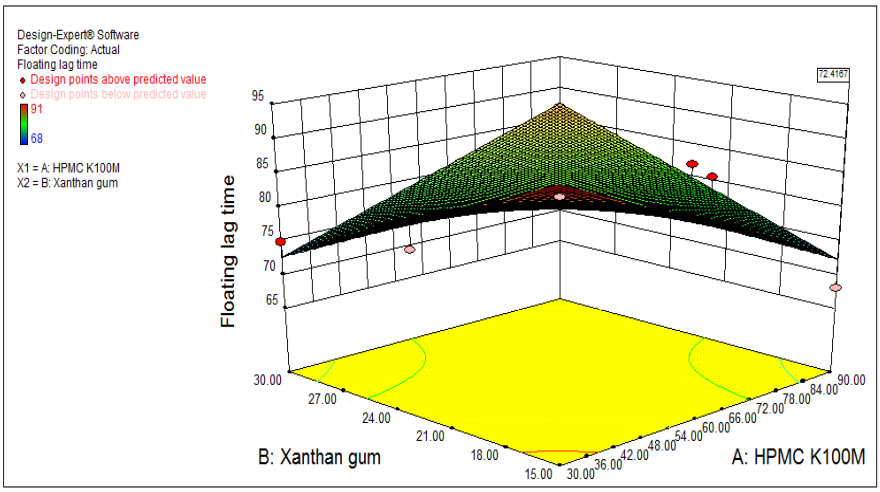

Figure 4: 3-D graph showing effect of HPMC K100 & Xanthan gum on Floating lag time.

Model for % Swelling Index.

After putting the data in Design Expert Software, fit summary applied to data in that linear model had been suggested by software.% Swelling Index follows linear model.

% Swelling Index = -0.264 - 0.042 HPMC K100M – 0.084 Xanthan gum

1.2666 HPMC K100M * Xanthan gum.

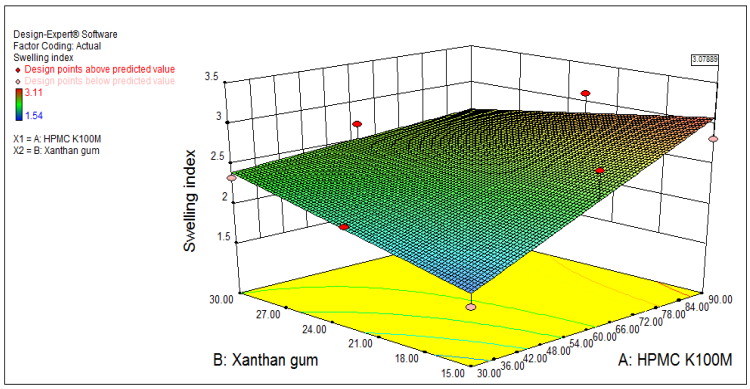

Figure 5: 3-D graph showing effect of HPMC K100 &Xanthan gum on Swelling Index.

Model for % Cumulative drug release.

After putting the data in Design Expert Software, fit summary applied to data in that linear model had been suggested by software. % Cumulative drug release follows linear model.

% Cumulative drug release = 92.25 +0.26 HPMC K100M +0.54 Xanthan gum

-0.019 HPMC K100M * Xanthan gum.

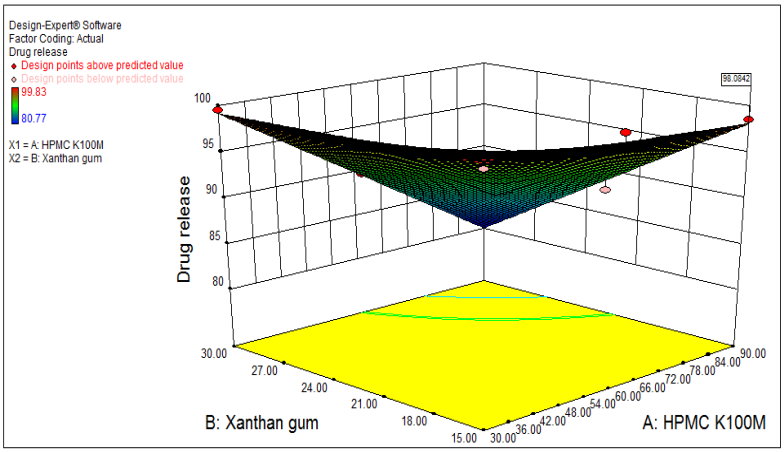

Figure 6: 3-D graph showing effect of HPMC K100 & Xanthan gum on % CDR

Graphical optimization

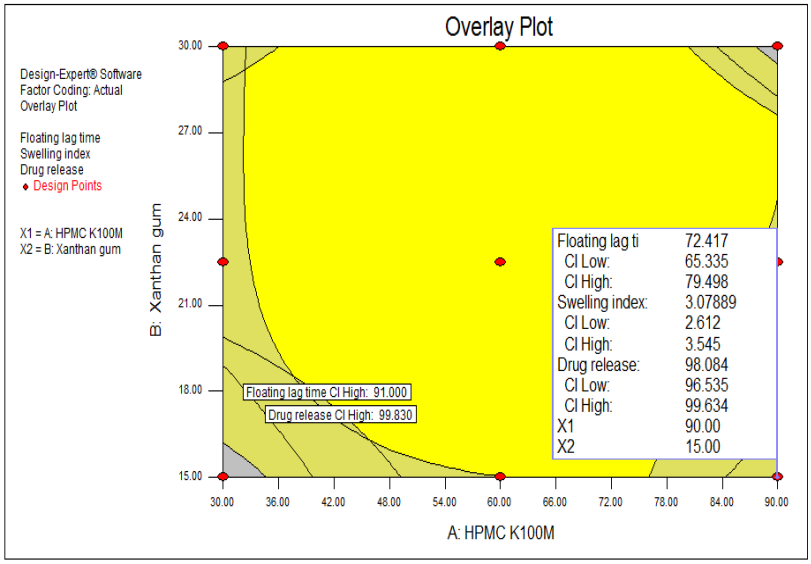

Figure 7: Graphical optimization of optimized formulation F6.

Graphical method of optimization was used for optimization and optimized point for the

Floating lag time 72.41 seconds

% Swelling Index 3.07 %

% Cumulative Drug Release 98.08 %

The level of variable at the optimized point

HPMC K 100 M = 90 mg

Xanthan gum = 15 mg.

Optimization Confirmation report.

Table 11: Confirmation result of optimized formulation

Two-sided		**Confidence = 95%**		**n = 1**		
Factor	Name	Level	Low Level	High Level	Std. Dev.	Coding
A	HPMC k 100	90	30	90	0	Actual
B	Xanthan Gum	15	15	30	0	Actual
Response	**Prediction**	**Std Dev**	**SE (n=1)**	**95%PI low**	**95%PI high**	
% Drug Release	98.08	0.92	1.20	94.99	101.17	
Swelling Index	3.07	0.27	0.36	2.14	4.00	
Floating lag time	72.41	4.21	5.48	58.30	86.52	

Confirmation report is shown in table no 8.21.

The report indicate that the factor A (HPMC K 100M) at 90 mg and factor B (Xanthan gum) at 15 mg gives the optimized formulation having point of prediction of

% Drug Release = 98.08 ± 0.92 %

% Swelling Index = 3.07 ± 0.27 %

Floating lag time = 72.41 ± 4.21 seconds

STABILITY STUDY

Table 12: stability studies of optimized formulation (F6).

Characteristic	**Initials**	**1 Month**	**2 Month**	**3 Month**
Hardness (kg/cm2)*	5.7 ± 0.27	5.83 ± 0.288	5.66±0.288	5.83± 0.288
Drug content Uniformity (mg/tablet)*	96.30 ± 0.10	95.00 ± 1.5	95.39±1.5	95.47 ± 1.32
Floating lag time (s)*	72 ± 1.52	75 ± 1.64	73 ± 2.00	75 ± 1.64
Total floating time (h)*	>24	>24	>24	>24
In vitro drug release at 12 hour*	98.08 ± 0.38	-	-	98.81 ± 0.11

*All the values are expressed as mean± S.D., n=3.

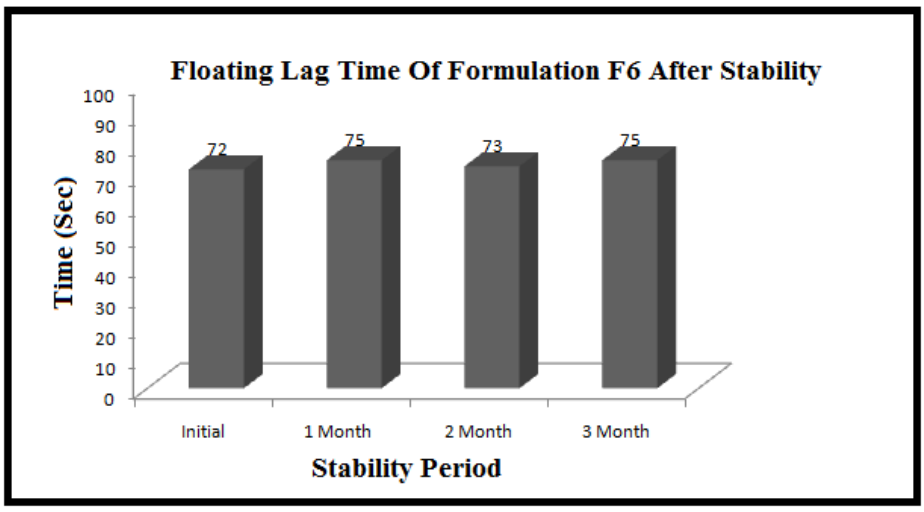

Figure 8 : Histogram for floating lag time of before and after stability studies for optimized formulation F6.

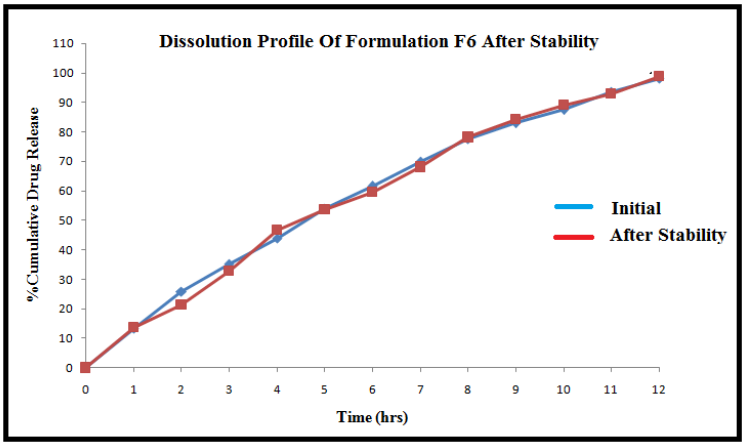

Figure 9: Comparisons for drug release profile of before and after stability studies for optimized formulation F6.

From the above figure there is no major difference was found between evaluated parameters before and after stability studies and all are in acceptable limits. The tablets showed satisfactory physical stability at 400C at 75 % RH.

CONCLUSION

The aim of the study was to study the effect of various hydrophilic polymers on in vitro release rate from gastro retentive floating tablet of Stavudine based on a low density polymer. The effervescent-based floating drug delivery was a promising approach to achieve *in vitro* buoyancy. Different types of matrix forming polymers- HPMC K100M and Xanthan gum were studied. Formulation F6 showed controlled drug release and adequate floating properties. The drug release from the tablets was sufficiently sustained and non- Fickian transport of the drug from tablets was confirmed. The stavudine floating tablets were stable at 40°C/75% RH up to 3 months.

REFERENCES

1. Dhirendra K, Vivek D, Shaila L, Brajesh P, Kavita R.G. and Sarvesh P. Design and evaluation of sustained release matrix once daily formulation of stavudine. Int J Drug Delivery 2010; 2:125-134.
2. Lachman L, Lieberman H.A. and Kanig J.L. The theory and practice of industrial pharmacy. 3rd edn., Varghese Publishing House, Mumbai, 1991;67-71:183-184, 296-302.
3. Rahul Thube, Suresh Purohit and Abhijit Gothoskar, Study of Effect of Custard Apple Pulp Powder As an Excipient on the Properties of Acetaminophen Tablet. World Applied Sci J 2011;12 (3): 364-371.

4. Patil SV, Kuchekar BS, Janugade BU, Lade PD. *In-Vitro* Studies of Stavudine Sustained Release from Hydrophilic Matrices. J Pharm Res, 2009;2(12):1855-1856.
5. Sonali S. Bharate, Sandip B. Bharateb and Amrita N. Bajaj, Interactions and incompatibilities of pharmaceutical excipients with active pharmaceutical ingredients: a comprehensive review, J. Excipients and Food Chem 2010;1 (3):3-26.
6. A. Pandey, B. Rath, A. K. Dwivedi, Review on pharmaceutical Preformulation studies with special emphasis on excipient compatibility. Int J Pharm Techno 2011;3(2):1029-1048.
7. Taufeeq Ali, Srinivas Mutalik, M. Venkatesh, Dinesh B Shenoy and N Udupa, Biodegradable implant of Gentamicin Sulphate for effective management of osteomyelitis. Saudi Pharma J 2006;14(2):120-125.
8. Sharma S, Sharma MC, Kohili DV, Chaturvedi SC. Formulation In-Vitro evaluation study of effect of hardness on buoyancy time of gatroretentive film and floating tablet. J optoelectronics and Biomedical Materials 2009;1(4):353-358.
9. Ferdous K, Shaikhul MIB, Ziaur RK, Kazi RA, Selim R. preparation and *In-Vitro* evaluation of theophyline loaded gastroretantive floating tablets of Methocel K4M. Dhaka Univ J Pharm Sci 2008;7(1):65-70.
10. Havaldar VD, Kulkarni AS, Dias RJ, Aloorkar NH, Mali KK. Floating matrix tablets of atenolol: Formulation and *In-Vitro* evaluation. Asian J Pharma 2009:286-291.
11. Margret C, Chandramohan, Debjit, chiranjib, Jayakar B. and Sampathkumar K.P. Design and characterization of sustain release gastroretantive floating tablets of diltiazim hydrochloride. Der Pharmacia Lettre 2009, 1(2), 25-38.
12. Julijana K, Sasa B, Franc V, Polona V. and Bojan Z. Optimisation of floating matrix tablets and evaluation of their gastric residence time. Int J Pharma 2000;195:125–135.
13. Ziyaur R, Mushir A, Khar RK. Design and evaluation of bilayer floating tablets of Captopril. Acta Pharm, 2006;56:49–57.
14. Singh B, Chakkal SK, Ahuja N. Formulation and optimization of controlled release mucoadhesive tablets of atenolol using response surface methodology. AAPS PharmSciTech 2006; 7(1):E1-E9.
15. Qazi S, Samuel KN. Evaluating dissolution profile of anti – HIV agent using ANOVA and non – linear regression model's in JMP software, Int J Pharma 2003; 252 :27–39.
16. Manavalan R, Ramasamy S. Physical Pharmaceutics: Accelerated Stability Testing. 1st edn., Vignesh Publisher, Chennai, 1995:288-299.

17. ICH Harmonized Tripartite Guideline, Stability Testing of New Drug Substances And Products, Q1A.(R),2000.
18. Amit Bhat, Chowdary KPR, Shobharani RH. Formulation and Evaluation of chronopharmaceutical Drug Delivery of Theophylline for Nocturnal Asthma , Int J Pharm Pharm Sci 2011; 3,(2):183-185.