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Original Article

Floating Extended Release Tablets of Tenofovir Formulation and Design by Central Composite Design (CCD) Using Cetyl Alcohol as Floating Assistant

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ABSTRACT

Introduction: The Tenofovir (TFR) is a BCS Class III widely prescribed treatment of HIV and Hepatitis. **Materials and Methods:** The CCD was used to statistically optimization parameters and evaluate on the efficacy of gastro retentive floating behaviour. The concentration of HPMC K100 M (X1), Cetyl Alcohol (X2) and Ethyl Cellulose (X3) were selected independent variables. To determine the following: drug release kinetics, counter and 3D surface plots, *in vitro* dissolution and comparison of TenoHep with optimized and F1 Formulation, swelling-erosion index, floating attributes and tablet properties. **Results:** The formulation R^2 was higher when fitted to zero order equation which indicates that a zero order release, except F12 as first order. **Conclusion:** The optimization floating is well suitable for gastro retentive following extend release.

Keywords: TenoHep, Tenofovir, Floating, Optimization, *In vitro*.

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INTRODUCTION

Tenofovir is classified as a BCS Class III drug with poor permeability and high solubility according to recent literature,[1] a novel TFR with stability has been developed as an alternative one. Nowadays, antiretroviral drugs can be given vaginally in a number of dosage forms, such as films. In particular, films that allow for controlled release were created, along with glycerol, triethyl citrate, and chitosan.[2,3]

The Polycaprolactone (PCL) fibers were electrospun, and their pharmacokinetics were assessed in mice.[4] They were also developed as a potential microbicide, sustained-release vaginal compacts with two release controls,[5] a prototype chitosan-based Nanoparticle (NP) anti-HIV microbicide,[6] TDF's Intravaginal Ring (IVR) formulation shows promise for increasing adherence and effectiveness,[7] obtained from niosomes using a high-pressure homogenizer,[8] the production of controlled-release, freeze-dried, bioadhesive vaginal bigels for tenofovir,[9] and the distribution of tenofovir and efavirenz by integrating nanoparticles into polymeric films was developed.[10] The extended-release tablets made using hydrophilic polymers, such as HPMC K100, HPMC K15, and ethyl cellulose, have been documented.[11-14]

A CCD was described to optimize the formulation parameters and assess the effects of three independent components.[15-18] Numerous formulations with a single and combined effect of independent variables were reported by the various statistical researches, along with other formulations.[19-26] The experiments were conducted in every possible combination, and the CCD was utilized to assess the impact of three independent variables at five distinct levels. The concentrations of HPMC K100 M (X1), cetyl alcohol (X2), and ethylene cellulose (X3) were chosen as independent variables in this study. For every gastro retentive floating tablet of Tenofovir, the release was assessed by CCD using the dependent variables floating lag time (Y1), swelling index (Y2), DR (drug release) 1 hr (Y3), DR-3hr (Y4), DR-6hr (Y5), T100 (Time necessary for 100% Drug Release) (Y6).

Every response and independent variable has been coded, and the exact levels are described in the Table 1. Each factor was assigned to five levels, which are the factorial point and central points (-α, -1, 0, 1, +α). Based on the fundamental composite design that the design expert software produced. Tenofovir gastro-retentive floating tablets trials totalling fifteen.

MATERIALS AND METHODS

Tenofovir A Gifted sample from Laurus Lab Pvt. Ltd., Viskhapatanam, HPMC K100 Gifted sample Colorcon Asia Private Limited, Varna, Goa, Cetyl alcohol, Ethyl cellulose, Megnesium Stereate and Talc was purchased from Loba Chemie Pvt. Ltd., Mumbai, Sodium Hydrogen Carbonate Purchased from Merck life science Private Limited.

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Development of Tablets

Based on an experimental design employing the central composite design shown in Table 1 and Table 2, the tablet was made by using the direct compression approach. The drug, HPMC K100 (X1), Cetyl alcohol (X2),[31] Ethyl cellulose (X3). Magnesium Stearate and Talc were then combined with M.C.C. 102 and other excipients before being well blended. The rotary compression machine (MN Enterprise) was used to compress the mixture of ingredients into tablets.

Evaluation of the tablets

The tablet preparations were tested for the amount of active component, hardness, friability, rate of dissolution, swelling index, buoyancy, dissolution.

Content of active ingredient

In a boiling test, the tablet powder corresponding to 50 mg of Tenofovir was used, and 6-10 mL of methanol was used to extract it. The methanolic extract was collected into a 100 mL volumetric flask, diluted with 0.1N hydrochloric acid buffer to make 100 mL, and its drug concentration was determined using a UV spectrophotometric technique.

Hardness

The hardness is determined by Monsanto hardness tester.

Friability

Friability was determined by Lab India tablet friability tester (FT 1020).

Dissolution Study

The tablet formulation was tested for dissolution using a USP type II (LABINDIA DS 8000) using 0.1N hydrochloric acid buffer as the dissolving fluid at a constant temperature of 37°C and 50 rpm throughout the investigation. The sample (5 mL) was collected at various times, including 1.0, 2.0, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5 and 7 hr, respectively. The samples were examined using at 260nm by UV method. The dissolution of each produced tablet was replicated (n=4).

In vitro Buoyancy study

It was visually evaluated in triplicate whether the tablets floated. The USP dissolution device with 0.1N hydrochloric acid buffer (kept at 37°C±0.50°C) was used to measure the floating time and the total floating time. The total floating time was the time, floating on the medium's surface (n=4).

Swelling studies

Matrix In order to measure swelling also known as water absorption capacity petri dish with a glass plate holding the tablet was utilised. The tablets were placed in a petri dish with 50 mL of medium at a temperature of 37°C±0.5°C, tablet was removed, blotted with absorbent tissue to remove dissolution medium and weighed.

Comparison of Optimized Formulation and F1 with Marketed Formulation

The comparison of marketed tablet with optimized and F1 Formulation given TenoHep 300 mg. Each Film coated mouth dissolving tablet contains Tenofovir IP 300 mg. Manufactured in India by Cadila Healthcare Ltd., Plot no. 203-213, Kundaim Industrial Estate, Kundaim, Goa-403 115 and Marked by Zydus Heptiza (A div of Cadila Healthcare Ltd.,) Batch no. G102238.

Data Analysis

Data analysis as per first order model and zero order, Higuchi and Pappas model. The dissolution parameters such as Swelling Index (%), Floating Lag time (Sec), % DR 1 hr, % DR 3 hr, % DR 6 hr, T100 are subjected to ANOVA (Analysis of Variance), 3D surface plots, Counter plots, desirability and other statistical parameter by using design Expert.

RESULTS AND DISCUSSION

Analytical method

The determination of drug concentration in samples was linear Y=0.013x+0.004 in the concentration range of 10 µg/mL to 60 µg/mL with R^2=0.998.

Tablet Properties

1. The hardness of all the tablets formulas for within the range 4.5 to 5.5 kg/cm^2 respectively. The increase hardness relevant binding properties of Tenofovir tablets.
2. The friability test is useful to obtain physical strength of tablets are the prepared formulation within the pharmacopeia standard % weight loss not exceeding 1%.
3. The drug content of all prepared tablets within the range of from 98 to 99% in the above quality control parameters of the prepared tablets fulfill official specification.
4. The floating behaviour of prepared tablets as giving in the Table 3 from F1 to F15.
5. The swelling behaviour study of the tablets was performing in 0.1 N Hydrochloric acid buffer and results indicating significantly change the swelling behaviour was found in F1 to F15.

In vitro dissolution

The formulation F1 maximum (100%) drug release 7.5 hr, F2 maximum drug release 7.5 hr, F3 maximum drug release 4.0 hr, F4 maximum drug release 6.5 hr, F5 maximum drug release

7.5hr, F6 maximum drug release 7hr, F7 maximum drug release 7.5 hr, F8 maximum drug release 7.5 hr, F9 maximum drug release 6 hr, F10 maximum drug release 6 hr, F11 maximum drug release 7.5 hr, F12 maximum drug release 6 hr, F13 maximum drug release 6 hr, F14 maximum drug release 5.5 hr, F15 maximum drug release 6 hr. The increasing order of drug dissolution of various formulations are shown F1=F5= F7= F8= F11=F2>F6>F4>F9=F10= F12=F13=F15> F14>F3.

Drug release

The drug release kinetic were performed to the data obtain from *in vitro* drug release studies shown in Figures 1-4. It was observed that the formulation R^2 was higher when fitted to zero order equation which indicates that a zero order such as F1, F2, F3, F4, F5, F6, F7, F8, F9, F10, F11, F13, F14, F15 .The first order release from the formulation such as F12.The release exponent (n) formulation F2, F3, F10, F14, F15 found to be non fickain diffusion. The release exponent (n) formulation F1, F4, F5, F6, F7, F8, F9, F11, and F13 found to be fickain diffusion. The

Table 1: Central Composite Design (CCD).

Factors	Levels					
Code level	(-)α	(-1)	0	1	(+)α	
X1	93.1821	98.1079	110	121.892	126.818	
X2	16.591	19.054	25	30.946	33.409	
X3	26.591	29.054	35	40.946	43.409	
Response	Constrains					
			-	+	Goal	
X1			100	120	116.955	Range
X2			20	30	20	Range
X3			30	40	40	Range
Y1			11	20	15.324	Range
Y2			55.952	65.780	61.2984	Range
Y3			16.25	52.38	22.8171	Range
Y4			31.356	78.038	52.3316	Range
Y5			71.87	100	78.29	Range
Y6			6	12	8.25075	Maximize

Table 2: Coded Levels as per CCD of Gastro Retentive Floating Tablets.

Formulations	X1	X2	X3
F1	0	0	0
F2	0	(+)α	0
F3	1	1	-1
F4	0	0	(-)α
F5	0	0	0
F6	(-)α	0	0
F7	0	0	0
F8	0	0	0
F9	-1	1	1
F10	1	-1	1
F11	0	0	0
F12	0	0	(+)α
F13	0	(-)α	0
F14	(+)α	0	0
F15	-1	-1	-1

(correlation coefficient) 'r' and reaction rate constant are shown in the Tables 4 and 5.

Comparative Studies

The comparative studies with optimized tablets and F1 with marketed tablets (TenoHep-500 mg). The marketed tablets 100% drug release within 10 min.

Data Analysis

The five responses such as Y1, Y2, Y3, Y4, Y5 and Y6 (T100 time req to 100% of drug release), were selected for statically optimization and fitted to specific model. The model comparison of different response shown in Tables 7-10.

Table 3: Characteristics of Tenofovir Floating Tablets F1 to F15 (*n*=3) Mean±SD.

Formulations	Hardness (Kg/cm²)	Friability (%)	Drug Content Uniformity (%)	Floating Lag Time (Sec)	Sweling Index (%)	%Drug Release in 6 hr	Total Floating time (hr)
F1	4.5±0.0321	0.85±001	98.8±015	19.08±0.01	52.11±0.01	87.74±0.011	18.1±0.077
F2	4.8±0.0145	0.75±0.01	99.0±0.023	20.07±0.011	62.386±0.022	87.970±0.022	16.22±0.04
F3	5.2±0.0134	0.76±0.23	98.9±0.034	19.52±0.087	57.82±0.033	100±0.00	20.01±0.002
F4	5.4±0.0111	0.82±0.21	99.2±0.054	21.32±0.034	58.54±0.044	75.44±0.01	22.12±0.011
F5	4.5±0.0123	0.85±0.045	98.8±0.065	19.08±0.023	61.78±0.044	87.742±0.011	18.01±0.02
F6	4.8±0.0123	0.86±0.05	99.4±0.022	18.18±0.098	62.386±0.044	92.520±0.011	10.02±0.022
F7	4.5±0.0421	0.85±0.054	98.8±0.043	19.08±0.022	59.565±0.044	87.742±0.011	18.02±0.023
F8	4.5±0.032	0.85±0.67	98.8±0.065	19.08±0.033	62.386±0.055	87.7±0.022	18.10±0.023
F9	5.2±0.021	0.77±0.544	99.5±0.088	20.04±0.045	62.386±0.066	100±0.00	21.01±0.11
F10	4.6±0.0321	0.78±0.0443	99.6±0.092	23.32±0.033	55.952±0.0111	100±0.00	19.23±0.033
F11	4.5±0.0121	0.85±0.0445	98.8±0.034	19.08±0.044	61.989±0.055	87.74±0.011	18.45±0.045
F12	5.2±0.0122	0.82±0.0776	99.4±0.056	18.46±0.088	62.386±0.033	100±0.00	19.20±0.034
F13	4.6±0.0221	0.81±0.044	98.9±0.034	19.06±0.087	57.10±0.022	100±0.00	15.01±0.022
F14	4.8±0.021	0.83±0.011	99.0±0.065	20.38±0.077	65.786±0.011	100±0.00	16.34±0.034
F15	4.8±0.011	0.82±0.022	99.7±0.089	20.55±0.022	61.357±0.033	100±0.00	18.23±0.023
Optimize	5.2±0.021	0.81±0.054	99.7±0.045	21.58±0.011	62.861±0.044	90.122±0.011	14.23±0.003

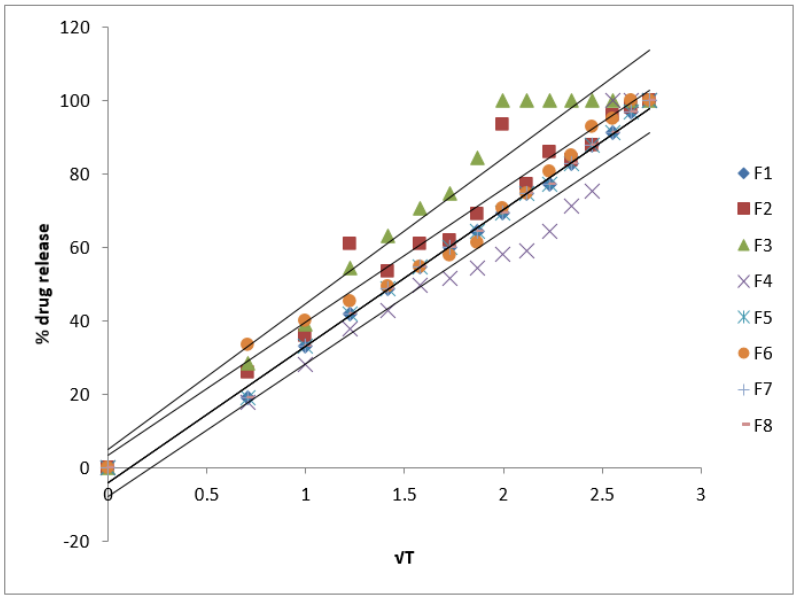

Figure 1: Higuchi model of Tenofovir F1 to F8 (*n*=3).

1. **Y1:** A model with statistically significant result $p<0.0001$ shown in Table 6. The parameters Floating lag time can be described by the model equation:

Y=-276.81813+ 3.65690 X1+ 4.38038 X2+ 1.77101 X3 -0.042929 X1X2 +0.020000 X1X3 0.028284 X2X3 -0.008241 X12 -0.012963 X22 -0.002963+ X32

The positive sign of 3 factors with increase floating lag time.

2. **Swelling Index (Y2):** The analysis of variance of swelling index. A model with statistically significant result $p<0.0001$ shown in the Table 7. The parameters swelling index can be described by the model equation:

Table 4: Coefficient of (r) Tenofovir F1 to F15 and Optimized (*n*=3) Mean±SD.

Formulation	Zero Order	First Order	Higuchi model	Peppas model
F1	0.9730±0.0221	0.9145±0.077	0.9981±0.011	0.9145±0.0043
F2	0.9200±0.0123	0.9041±0.0123	0.9616±0.077	0.5959±0.0221
F3	0.9745±0.055	0.8414±0.033	0.8412±0.0123	0.5519±0.0123
F4	0.9517±0.0123	0.7295±0.011	0.9668±0.0221	0.6465±0.012
F5	0.9730±0.066	0.9145±0.0221	0.9981±0.055	0.9145±0.0123
F6	0.9658±0.0221	0.8978±0.032	0.9879±0.0443	0.6102±0.0987
F7	0.9730±0.011	0.9145±0.045	0.9981±0.0221	0.9145±0.011
F8	0.9730±0.0221	0.9145±0.0221	0.9981±0.0213	0.9145±0.0221
F9	0.9383±0.099	0.8980±0.0321	0.9958±0.0321	0.5767±0.0065
F10	0.9739±0.0123	0.9125±0.0123	0.9972±0.0123	0.6549±0.0123
F11	0.9730±0.0123	0.9145±0.034	0.9981±0.0543	0.9145±0.001
F12	0.8368±0.077	0.8808±0.0221	0.9107±0.0321	0.4672±0.002
F13	0.9425±0.0123	0.9015±0.042	0.9942±0.0221	0.6017±0.0221
F14	0.9538±0.0221	0.8383±0.088	0.9459±0.0123	0.5980±0.0123
F15	0.9798±0.001	0.8613±0.022	0.9865±0.0221	0.6302±0.066
Optimize	0.9060±0.002	0.9571±0.0123	0.9896±0.0112	0.6604±0.0221

Table 5: Reaction rate constant of Tenofovir gastro retentive Floating tablets of Formulation F1 to F15 AND Optimized (*n*=3) Mean±SD.

Formulation	(K_o)	(K_1)	(K_H)	(K_P)	'n' (Diffusion Exponent)
F1	8.914±0.0221	0.2441±0.065	35.7819±0.077	0.5159±0.034	0.1518±0.0021
F2	1.52±0.0023	0.3638±0.0221	45.8837±0.0332	0.5985±0.012	0.7324±0.0023
F3	17.222±0.00231	0.3039±0.032	1.593±0.0321	0.454±0.0023	0.512±0.032
F4	9.862±0.0321	0.0736±0.001	40.7489±0.002	0.6604±0.034	0.202±0.044
F5	8.914±0.0432	0.2303±0.05	35.7819±0.0023	0.5159±0.011	0.1518±0.054
F6	11.042±0.0221	0.2441±0.0023	33.079±0.033	0.4747±0.022	0.2651±0.011
F7	8.914±0.011	0.2441±0.078	35.7819±0.022	0.5159±0.043	0.1518±0.054
F8	8.914±0.0432	0.2441±0.0221	35.7819±0.021	0.5159±0.0221	0.1518±0.022
F9	7.986±0.0123	0.2026±0.0023	57.781±0.09	0.3818±0.023	0.3886±0.033
F10	9.344±0.0987	0.2533±0.0654	33.648±0.0221	0.454±0.022	0.6206±0.003
F11	8.914±0.0023	0.2441±0.0321	35.7819	0.5159±0.006	0.1518±0.02
F12	13.18±0.0221	0.4283±0.0765	83.469±0.054	0.9287±0.065	0.3661±0.001
F13	11.658±0.0231	0.26.25±0.0432	34.7273±0.0023	0.4127±0.0023	0.2413±0.0023
F14	12.83±0.090	0.373±0.033	45.3744±0.011	0.5779±0.076	0.625±0.003
F15	21.866±0.066	0.0783±0.0221	57.693±0.0221	0.5056±0.0221	0.7324±0.0023
Optimize	2.92±0.0221	0.1427±0.021	44.0086±0.076	0.4844±0.011	0.3946±0.0221

Y=17.25639 - 0.091503 X1 - 0.332623 X2 - 0.027784 X3+ 0.001553 X1X2 -0.002796+ X1X3+ 0.001000 X2X3+ 0.000713 X12+ 0.002186 X22 + 0.004408 X32

Due to decrease swelling index.

3. **Y3:** A model with statistically significant result P≤0.6773 % drug release in 1hr shown in Table 8. The parameters %drug release in 1hr can be described by the model equation:

Y=-15.89414+ 0.055204 X1+ 0.067001 X2+ 0.956647 X3+0.003851 X1X2- 0.006095 X1X3 - 0.003352 X2X3+ 0.000219 X12 - 0.008202 X22- 0.002880 X32

Positive sign indicates increase release.

4. **(DR) % drug release in 3 hr (Y4):** A model with statistically significant result P≤0.4582 drug release in 1hr. The parameters % drug release in 3hr can be described by the model equation:

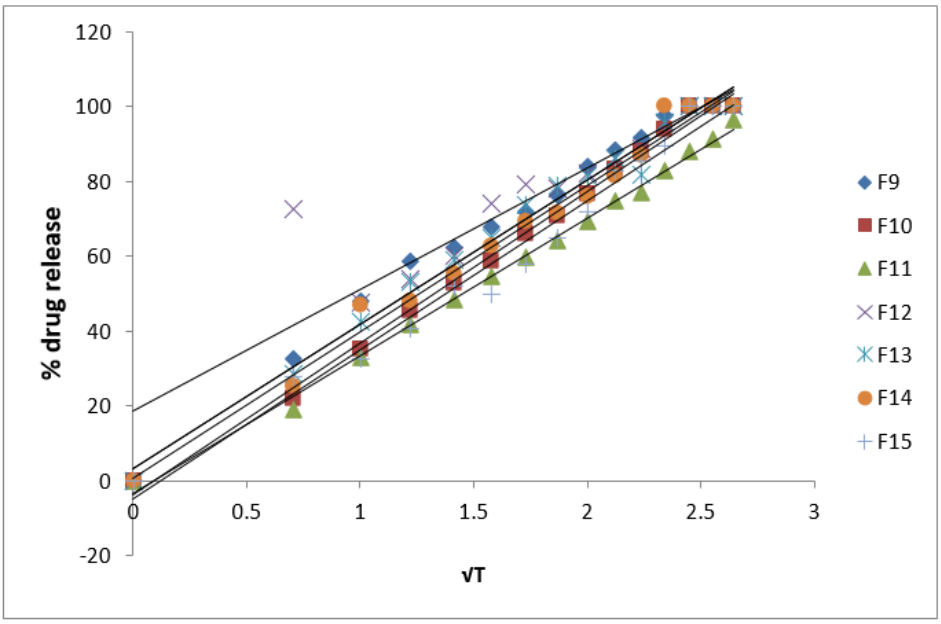

Figure 2: Higuchi model of Tenofovir F9 to F15 (*n*=3).

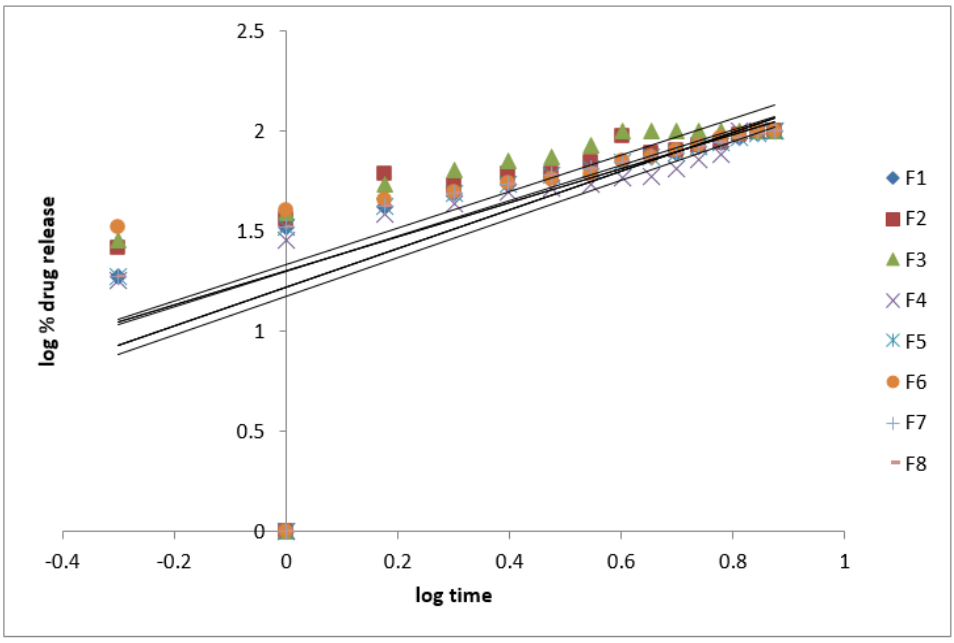

Figure 3: Peppas Model of Tenofovir F1 to F8 (*n*=3).

Table 6: Model comparison of response (Y1) Floating Lag time.

Source	Sequential *p*-Value	Lack of Fit *p*-Value	Adjusted R^2	Predicted R^2	Remark
Mean	<0.0001				Suggested
Linear	0.4714	0.6720	-0.0216	-0.3910	

Table 7: Model comparison of response (Y2) Swelling Index. Transform: Square Root

Source	Sequential *p*-Value	Lack of Fit *p*-Value	Adjusted R^2	Predicted R^2	Remark
Mean	<0.0001				Suggested
Linear	0.7370	0.6599	-0.1397	-0.5907	
2FI	0.7198	0.5163	-0.3378	-4.5657	
Quadratic	0.3132	0.8068	-0.1122	-0.3086	
Cubic	0.8068		-3670		Aliased

Table 8: Model comparison of response (Y3) DR 1 hr. Transform: Natural Log

Source	Sequential *p*- Value	Lack of Fit *p*-Value	Adjusted R^2	Predicted R^2	Remark
Linear	0.6773	0.5019	-0.1147	-0. 5982	
2FI	0.4623	0.4557	-0.1309	-0. 9639	
Quadratic	0.3238	0.5243	0.0455	-3. 4478	Suggested
Cubic	0.5243		-0.0640		Aliased

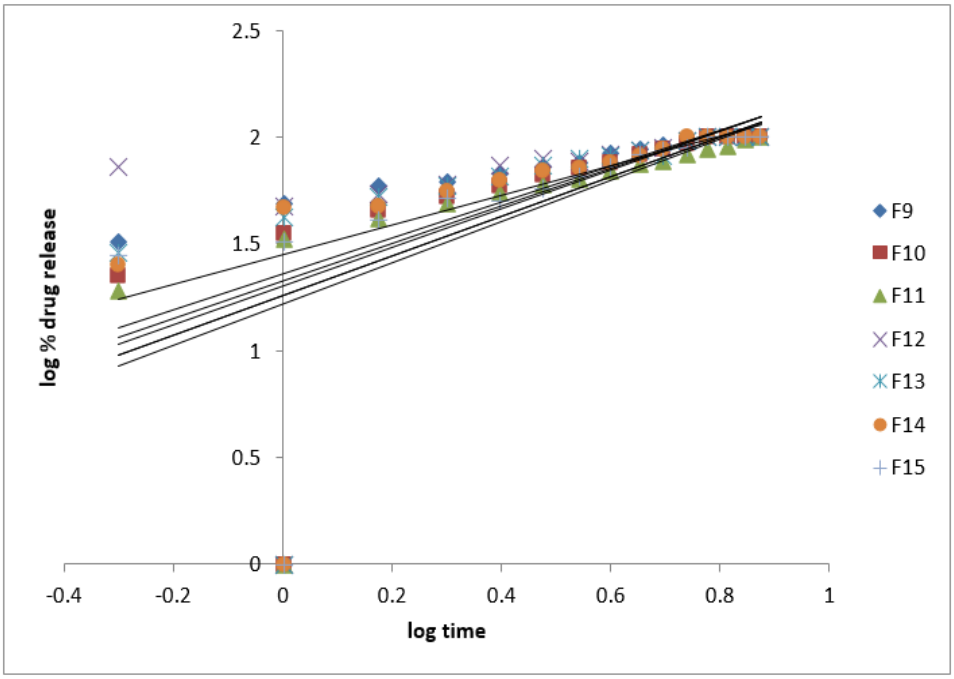

Figure 4: Peppas Model of Tenofovir F9 to F15 (*n*=3).

Y=-518.21471+ 4.71203 X1+19.16846 X2+5.89623 X3--0.066144

X1X2+ 0.011533 X1X3+ 0.089837 X2X3 -0.017085 X12 -0.335680

X22 -0.132440 X32

Positive sign indicates increase drug release.

5. **(DR) % drug release in 6 hr (Y5):** A model with statistically significant result P≤ 0.5316. % drug release in 1hr shown in Table 9. The parameters % drug release in 3hr can be described by the model equation:

Y=951.27691 -9.37822 X1 -13.80045X2 -8.93794 X3+ 0.182086 X1X2+ 0.120402 X1X3-0.164840 X2X3

Negative sign indicates that the decreased decrease drug release.

5. **Y6:** A model with statistically significant result $p \leq 0.0061$ time req for 100% drug release shown in Table 10. The parameters Time req for100% drug release for 100% drug release can be described by the model Equation:

Y=-6.63380+ 0.094347 X1+0.197916 X2+0.055709 X3 -0.000733 X1X2+0.000052 X1X3+ 0.003087 X2X3 -0.000350 X12 -0.000268 X22 + 0.000214 X32

Positive sign indicates increase release.

DISCUSSION

The *in vitro* dissolution profile of prepared gastro retentive tablets was shown in the Figures 5 and 6. The F1 100% drug release in 7.5 hr and optimize 100% drug release in 8.5 hr so that the comparison of marketed tablet with F1 and optimize were not identical dissolution data Shown in Figure 7. The model comparison of different response shown in Table 6 to Table 8. The desirability concern was found to be higher (0.606) for the optimize formula indicating suitability of the formulation.[27-35]

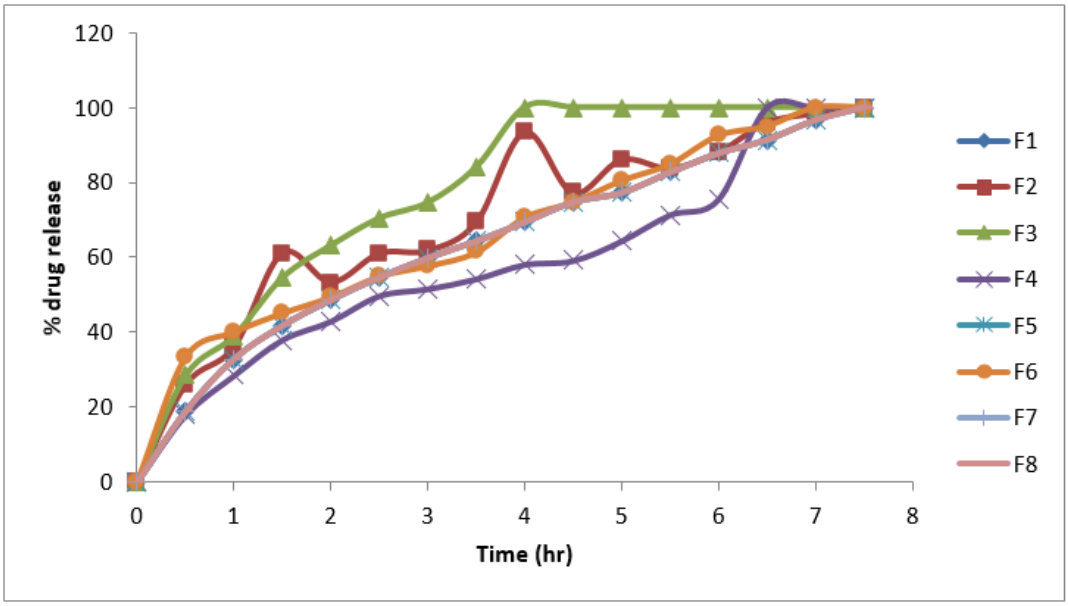

Figure 5: Mean Dissolution Profile of Tenofovir Formulation F1 to F8 (*n*=3).

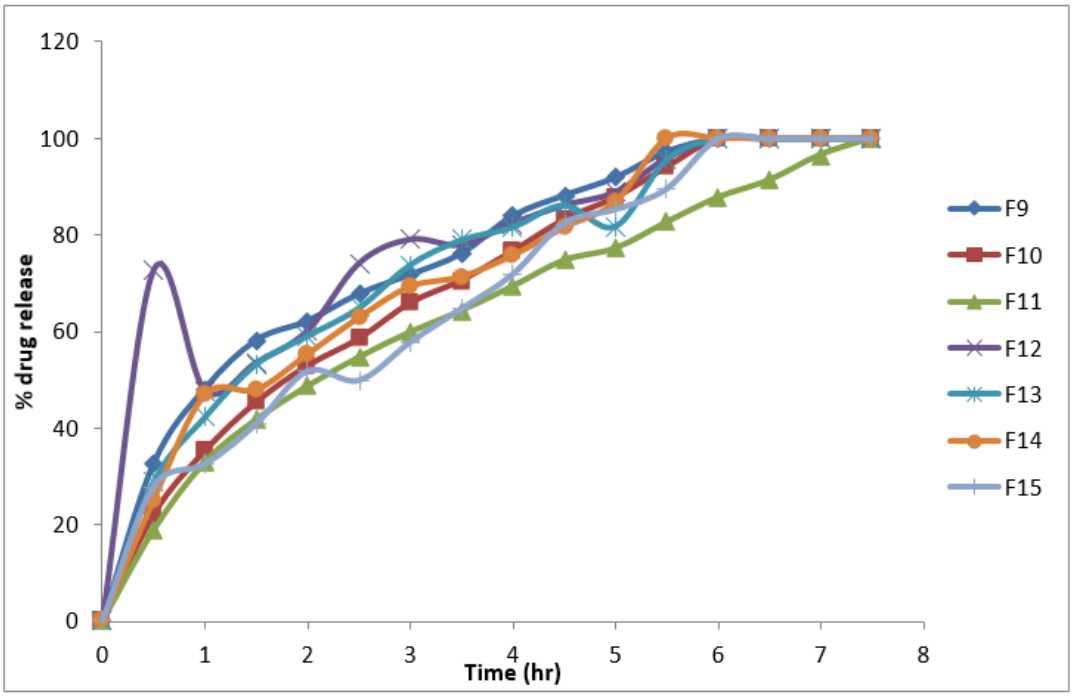

Figure 6: Dissolution Profile of Tenofovir Formulation F9 to F15 (*n*=3).

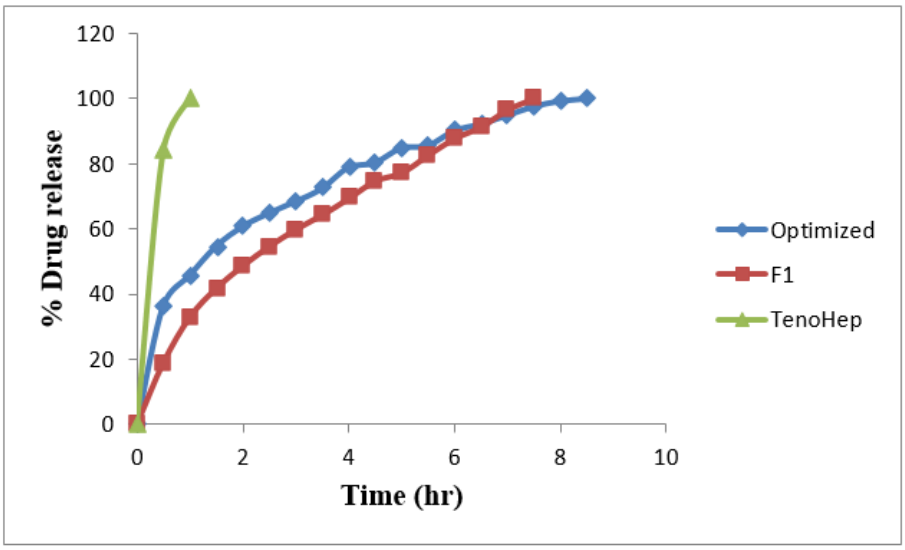

Figure 7: Dissolution Profile of F1, Marketed and Optimized Formulation (*n*=3).

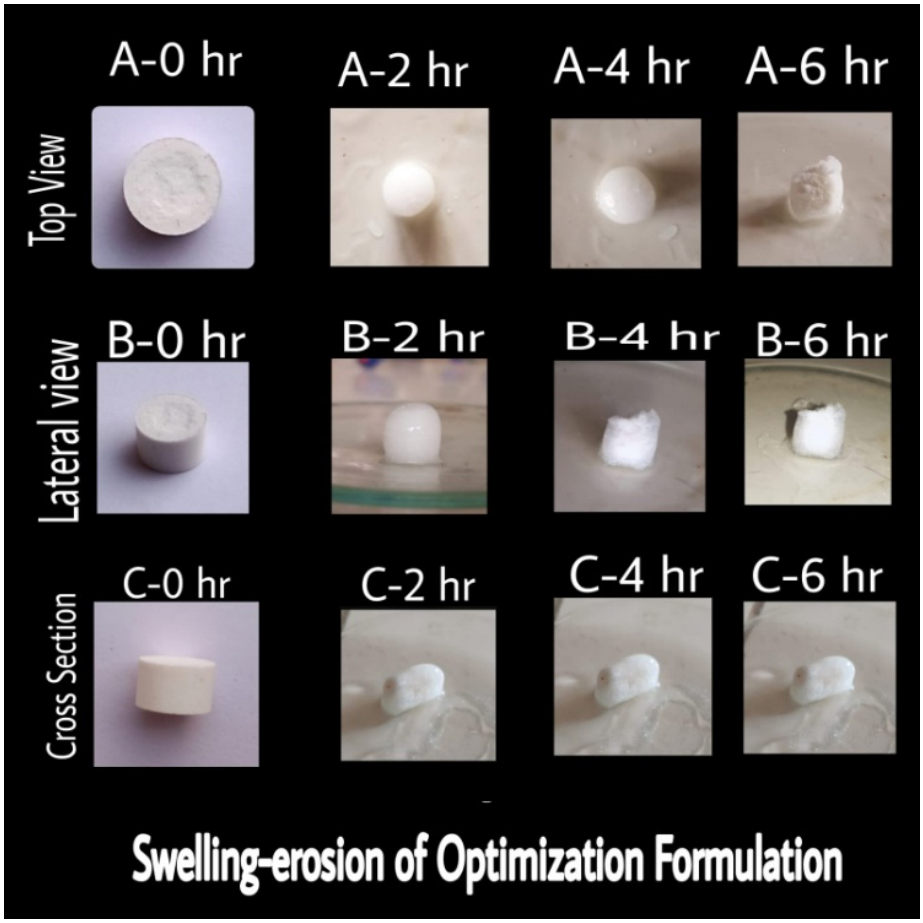

Figure 8: Swelling-erosion of Optimization Formulation.

Each response optimizes with desire target adjusted was set to be ranged, Floating lag Time (Y1) Swelling Index (Y2) was set to be range, and % Drug release in 1 hr (Y3) was Set to be range, % drug release in 3 hr (Y4) was set to range, % drug release in 6 hr (Y4) was set to range, T100 Time req for the 100% drug release (Y6) was set to be maximized. Six independent variables for optimize in according with the goal of response by adopting a desirability function the composition of optimized formulation was shown in the Table 1. In which X1, X2, and X3 were 116.955 mg, 20 mg, 40.00 mg respectively with corresponding desirability

function (0.606). The Optimize formulation gave, Floating lag time (21.58 sec), Swelling index (60.78) shown in Figure 8, % drug release in 1 hr (36.37%), % drug release in 3 hr (68.44%), % of drug release in 6 hr (90.122%). T100 Time req. for 100% drug release (8.5 hr) respectively. The drug release from the optimize formulation follow Higuchi model and follows Fickain diffusion. The optimized gastro retentive floating Tenofovir tablets are 100% drug release 8.5 hr well suitable for floating extended-release tablets. The contour plot, 3D Surface plot, Histogram and Swelling Index were shown in the Figures 9-13.

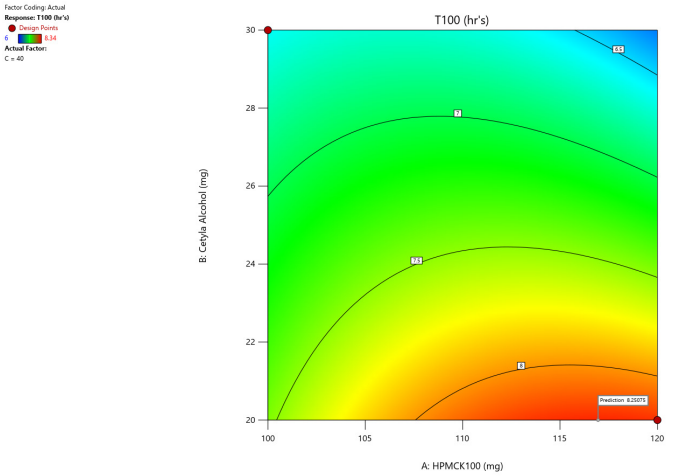

Figure 9: Counter plot of T100 Optimized.

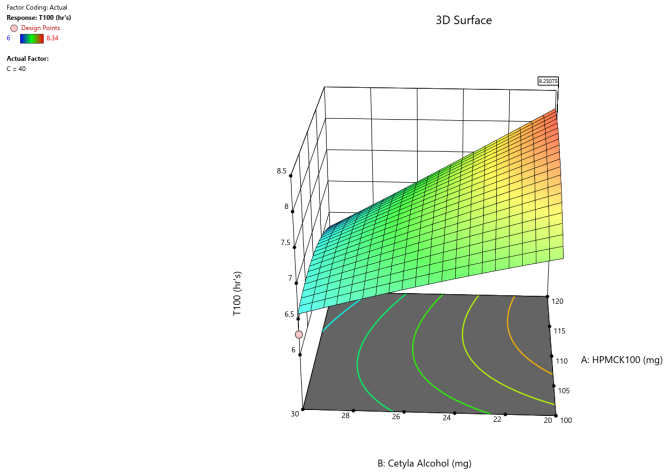

Figure 11: 3D Surface plot of T100 Optimized.

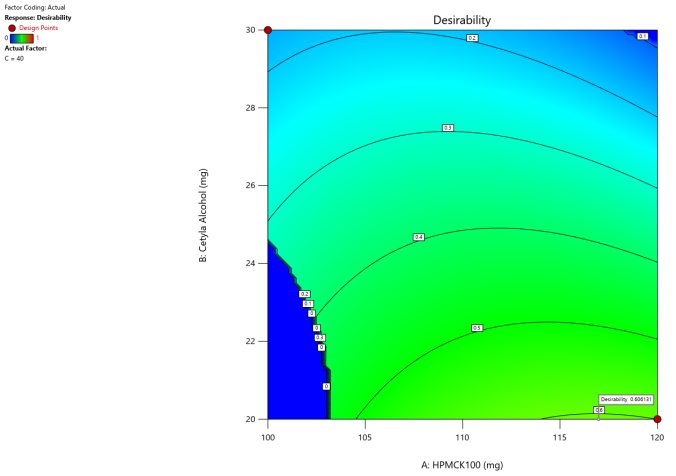

Figure 10: Counter plot of Desirability.

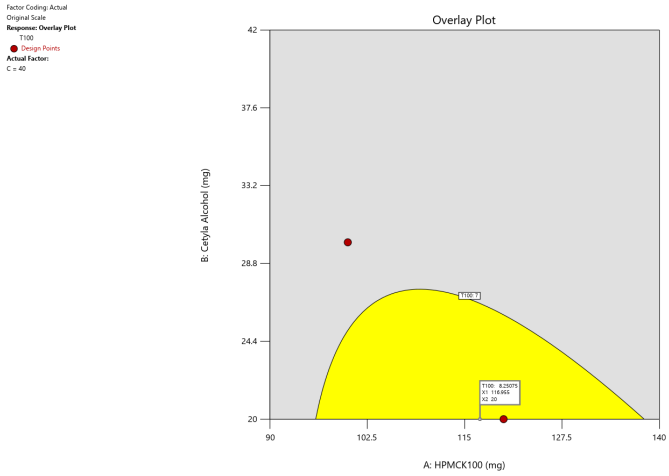

Figure 12: Overlayplot-Optimization.

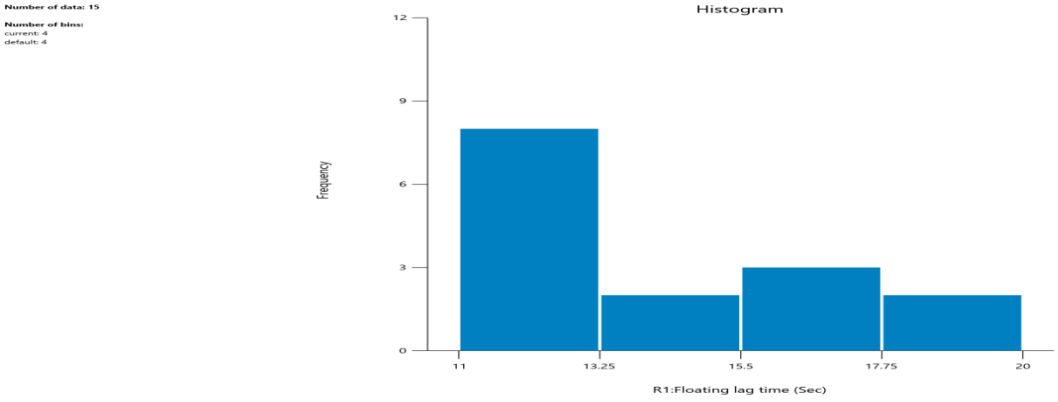

Figure 13: Histogram Floating Lag time (Sec).

CONCLUSION

The quality control parameter of the prepared tablets fulfils official specifications of tablets as per IP. The increasing order of drug dissolution of various formulation are F1=F5= F7= F8= F11=F2>F6>F4>F9=F10= F12=F13=F15> F14>F3. The formulation R^2 was higher when fitted to zero order indicates that a zero-order release from the formulation such as F1, F2, F3, F4, F5, F6, F7, F8, F9, F10, F11, F13, F14, F15 and first order such as F12.The comparison with optimize formulation, F1 and Market tablets dissolution profile not identical. The drug release from optimization formulation following First order Kinetic and fickain diffusion. The optimization floating is 100% is drug release within 8.5 hr is well suitable for gastro retentive following extend release.

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ABBREVIATIONS

BCS: Biopharmaceutical classification system; **CCD:** Central composite design; **HPMC:** Hydroxy propyl methyl cellulose; **DR:** Drug release; **MCC:** Microcrystalline cellulose; **QbD:** Quality by Design.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

CCD used to optimized process parameter of Tenofovir extended released tablets. The release of optimized formulation with fickain diffusion shown significant release profile with QbD approach with HPMCK100 and beneficiary for therapeutic use shown gastro retentive along with release profile as extended manner.

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