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Original Article

Formulation Development and Evaluation of Moxifloxacin.HCL Fast Dissolving Tablets

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ABSTRACT

The main objective of present research investigation is to formulate the Moxifloxacin.HCl Fast Dissolving tablets. Moxifloxacin.HCl, a synthetic fluoroquinolone antibacterial agent, and used to treatacute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis. The Fast Dissolving tablets of Moxifloxacin.HCl were prepared employing different concentrations of Crospovidone and Croscarmellose sodium in different combinations as a Superdisintegrants by Direct Compression technique using 3^2 factorial design. The concentration of Crospovidone and Croscarmellose sodium was selected as independent variables, X1 and X2 respectively whereas, wetting time, Disintegration time, $t_{50\%}$, and $t_{90\%}$were selected as dependent variables. Totally nine formulations were designed and are evaluated for hardness, friability, thickness, Assay, Wetting time, Disintegration time, *In-vitro* drug release. From the Results concluded that all the formulation were found to be with in the Pharmacopoeial limits and the In-vitro dissolution profiles of all formulations were fitted in to different Kinetic models, the statistical parameters like intercept (a), slope (b) & regression coefficient (r) were calculated. Polynomial equations were developed for Wetting time, Disintegration time, $t_{50\%}$, $t_{90\%}$. Validity of developed polynomial equations were verified by designing 2 check point formulations (C1, C2). According to SUPAC guidelines the formulation (F5) containing combination of 7.5% Crospovidone and 7.5% Croscarmellose, is the most similar formulation (similarity factor f2=68.88, dissimilarity factor f1= 3.35& No significant difference, t= 0.00354) to marketed product (AVELOX-400). The selected formulation (F5) follows First order, Higuchi's kinetics, mechanism of drug release was found to be Non-Fickian Diffusion Super Case-II Transport (n= 1.902).

Key words: Moxifloxacin.Hcl, 3^2 factorial Design, Super Disintegrates, Crospovidone, Croscarmellose Sodium, Wetting Time.

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INTRODUCTION

Researchers throughout the world are focusing intensively on the methods for the development of new drug delivery systems to enhance patient's compliance.Fastdissolving tablets become an emerging trend in the pharmaceutical industry. Fast dissolving tablets are ideal for all types of people, including for people who have swallowing difficulties, pediatric, geriatric, and bedridden patients. It is also for active patients who are busy, travelling and may not have access to water. Fast dissolving tablets are also known as orodispersible tablets, mouth-dissolving tablets, orally disintegrating tablets, melt-in mouth tablets, rapimelts, porous tablets, quick dissolving etc. Many drugs have the potentials to be made into orodispersible tablets.

Fast-dissolving drug-delivery systems were initially developed in the late 1970s as an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who experiences difficulties in swallowing traditional oral solid-dosage forms.[1] The speed of solubility of drug affects the rate of absorption of the drug. The faster the drug dissolve into solution, quicker the absorption and onset of clinical effect. They should readily dissolve or disintegrate in the saliva generally within<60 seconds. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. The significance of orodispersible dosage forms are progressively being recognized in both, industry and academics.The small volume of saliva isusually sufficient to result in tablet disintegration in the oral cavity. The medication can then be absorbed partially or entirely into the systemic circulation from blood vessels in the sublingualmucosa, or it can be swallowed as a solution to be absorbed from the gastrointestinal tract. Thesublingual route usually produces a faster onset of action than orally ingested tablets and theportion absorbed through the sublingual blood vessels bypasses the hepatic first-pass metabolicprocesses. The performance of ODT depends on the technology used in their manufacture. The orally disintegratingproperty of the tablet is attributable to a quick intake of water into the tablet matrix, which creates porous structures and resultin rapid disintegration. Hence the basic approaches to develop ODT include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent and using highly water soluble excipients in the formulation. Orally disintegratingtablets are formulated by utilizing several processes, which differ in their methodologies and the ODTsformed vary in various properties such as, mechanical strength of tablet, taste and mouth feel,swallow ability, drug dissolution in saliva, bioavailability and stability. Various processes employed informulating ODTs include Freeze-Drying or Lyophilization, cotton candy process, molding, spray drying,mass extrusion and compaction (wet granulation, dry granulation, and direct compression).

In the present study the direct compression method was adopted to manufacture the ODT tablets, since it was very simple and do not require any sophisticated equipment's. The direct compression represents the simplest and most costeffective tablet manufacturingtechnique.[2]

ODT by direct compression technique is a simple approach of drug delivery systems that proved to be rational in the pharmaceutical arena for its ease, compliance, faster production, avoid hydrolytic or oxidative reactions occurred during processing of dosage forms.

Drug Profile and Rationality for Experimental Design

Moxifloxacin is a fourth-generation synthetic fluoroquinolone antibacterial agent. It is used for the treatment ofacute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, community acquired pneumonia,complicated and uncomplicated skin and skin structure infections, and complicated intra-abdominal infections.[3]Moxifloxacin is a broad-spectrum antibiotic that is active against both Gram-positive and

Gram-negative bacteria. Itfunctions by inhibiting DNA gyrase, a type II topoisomerase, and topoisomerase IV, enzymes necessary to separate-bacterial DNA, thereby inhibiting cell replication. The half-life of moxifloxacin is 11.5-15.6 hours.

In case of chronic bronchitis, patients face difficulty in swallowing the conventional dosage form (tablets). Hence to overcome this problem, attempts will be made to formulate a Fast DissolvingTablets. This leads to an increase in bioavailability byavoiding first pass metabolism.[4]

It is an important issue is to design an optimized formulation with an appropriate dissolution rate in a short time period and minimum trials. Many statistical experimental designs have been recognized as useful techniques to optimize the process variables. For this purpose, response surface methodology (RSM) utilizing a polynomial equation has been widely used. Different types of RSM designs include 3-level factorial design, central composite design (CCD), Box-Behnken design and D-optimal design. Response surface methodology (RSM) is used when only a few significant factors are involved in experimental optimization. The technique requires less experimentation and time, thus proving to be far more effective and cost-effective than the conventional methods of formulating sustained release dosage forms.[5-8]

Hence an attempt is made in this research work to formulate Fast Dissolving Tablets of Moxifloxacin.HClusingCrospovidoneandCroscarmellosesodium. Instead of normal and trial method, a standard statistical tool design of experiments is employed to study the effect of formulation variables on the release properties.

Large scale production needs more simplicity in the formulation with economic and cheapest dosage form. The Fast Dissolving tablets formulation by direct compression method is most acceptable in large scale production.

A **3^2** full factorial design was employed to systematically study the drug release profile. A 3^2 full factorial design was employed to investigate the effect of two independent variables (factors), i.e the amounts of Crospovidone and Croscarmellose on the dependent variables, i.e. Disintegration time, Wetting Time, $t_{50\%}$, $t_{90\ \%}$,(Time taken to release 50%, 90% respectively)

MATERIALS AND METHODS

Materials used in this study were obtained from the different sources. Moxifloxacin.HClwas a gift sample from Dr.Reddy's Laboratories, Hyderabad, India. Emcompress, Crospovidone, Croscarmellose, were procured from LobaChemiePvt.Ltd, Mumbai. Other excipients such as Magnesium Stearate, talc and Aspartame were procured from S.D. Fine Chem. Ltd., Mumbai.

Formulation Development of Moxifloxacin.HCl Fast Dissolving Tablets

The factorial design is a technique that allows identification of factors involved in a process and assesses their relative importance. In addition, any interaction between factors chosen can be identified. Construction of a factorial design involves the selection of parameters and the choice of responses.[9-10]

A selected three level, two factor experimental design (3^2 factorialdesign) describe the proportion in which the independent variables Crospovidone and Croscarmellosesodium were used in formulation of Moxifloxacin.HClFast Dissolving Tablets. The time required for 50% ($t_{50\%}$), 90% ($t_{90\%}$) drug dissolution, Disintegration Time and Wetting Time were selected as dependent variables. Significance terms were chosen at 95% confidence interval ($p<0.05$) for Final Equations. Polynomial equations were developed for $t_{50\%}$, $t_{90\%}$, Disintegration Time and Wetting Time (step-wise backward Linear Regression Analysis).

The three levels of factor X1 (Crospovidone) at a concentration of 10%, 7.5%, 5%.Three levels of factor X2 (Croscarmellose) at a concentration of 10%, 7.5%, 5%. (% with respect to average weight of Tablet, i.e600 mg) was taken as the rationale for the design of the Moxifloxacin.HCl Fast Dissolving tablet formulation. Totally nine Moxifloxacin.HClFastDissolvingtablet formulations were prepared employing selected combinations of the two factors i.e, X1, X2 as per 3^2 Factorial and evaluated to find out the significance of combined effects of X1, X2to select the best combination and the concentration required to achieve the desired Fast release/ Dissolution of drug (by providing large Surface area and Improved Solubility) from the dosage form.

Preparation of Moxifloxacin.HCl Fast Dissolving Tablets

Moxifloxacin.HCl Tablets were prepared by direct compression method. The composition of each tablet is shown in Table 2. The drug, diluents, superdisitegrants were passed through sieve #40. All the above ingredients were properly mixed together (ina poly-bag). Talc and Magnesium stearate were passed through mesh #80, mixed and blended with initial mixture in a poly-bag. The powder blend was compressed into tablets on a 8 station rotary punch tableting machine (minipress) using 12 mm circular punches and same hardness was used for the required number tablets. Compressed tablets were examined as per official standards and unofficial tests. Tablets were packaged in well closed light resistance and moisture proof containers.

Experimental Design

Experimental design utilized in present investigation for the optimization of Superdisintegrant concentration such as, concentration of Crospovidone was taken as X_1 and concentration of Croscarmellose sodium was taken as X_2. Experimental design was given in the Table 1. Three levels for the Concentration of Crospovidone were selected and coded as -1= 5%, 0=7.5%, +1=10%. Three levels for the Concentration of Croscarmellose sodium were selected and coded as -1= 5%, 0=7.5%, +1=10%. Formulae for all the experimental batches were given in Table 2.[5-11]

Evaluation of Moxifloxacin.HCL Fast Dissolving Tablets

Hardness

The hardness of the tablets was tested by diametric compression using a Monsanto Hardness Tester. A tablet hardness of about 2-4 Kg/cm^2 is considered adequate for mechanical stability.[12]

Friability

The friability of the tablets was measured in a Roche friabilator (Campbell Electronics, Mumbai). 20 Tablets were taken, weighed and Initial weight was noted (W_0) arededusted in a drum for a fixed time (100 revolutions, in a Roche Friabilator) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 %.[12]

Friability (%) = [(Initial weight- Final weight) / (Initial weight)] x 100

Content Uniformity

In this test, 20 tablets were randomly selected and the percent drug content was determined, the tablets contained not less than 85% or not more than 17.5% (100±7.5%)of the labeled drug content can be considered as the test was passed.[13]

Assay

Drug content was determined by weighing randomly selected tablets, pulverizing to a fine powder. The powder equivalent to 100 mg Moxi-

floxacin.HClwas weighed and dissolved in 10 ml of Distilled water in volumetric flask, the volume was adjusted to 100 ml with Phosphate buffer pH 6.8and the solution was filtered. An aliquot of 1.0 ml of solution were diluted to 10 ml Phosphate buffer pH 6.8 in separate volumetric flask. The drug content in was determined spectrophotometric ally at 288 nm.[3-14]

Thickness

Thickness of the all tablet formulations were measured using vernier calipers by placing tablet between two arms of the vernier calipers.[12]

Wetting time

To measure Wetting time of the Tablet, a piece of Tissue paper folded twice was placed in a small petri dish (Internal Diameter is= 6.5 cm) containing 5 ml of Distilled water. A Tablet placed on the paper, and the time for complete wetting of the tablet was measured in seconds.[15-17]

In-vitro Dissolution Study

The *In-vitro* dissolution study for the Moxifloxacin.HCl Fast Dissolving tablets were carried out in USP XXIII type-II dissolution test apparatus (Paddle type) using 900 ml of Phosphate buffer pH 6.8 as dissolution medium at 50 rpm and temperature 37±0.5°C. At predetermined time intervals, 5 ml of the samples were withdrawn by means of a syringe fitted with a pre-filter, the volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium. The resultant samples were analyzed for the presence of the drug release by measuring the absorbance at 288 nm using UV Visible spectrophotometer after suitable dilutions. The determinations were performed in triplicate (n=3).

Disintegration test

Disintegration of fast disintegrating tablets is achieved in the mouth owing to the action of saliva, however Quantity of saliva in the mouth is limited and no tablet disintegration test was found in USP and IP to simulate *in vivo* conditions. A modified method was used to determine disintegration time of the tablets. A cylindrical vessel was used in which 10 mesh screen was placed in such way that only 2 ml of disintegrating or dissolution medium would be placed below the sieve. To determine disintegration time, 6 ml of Sorenson's buffer (pH 6.8), was placed inside the vessel in such way that 4 ml of the media was below the sieve and 2 ml above the sieve. Tablet was placed on the sieve and the whole assembly was then placed on a shaker. The time at which all the particles pass through the sieve was taken as a disintegration time of the tablet. Six tablets were chosen randomly from the composite samples and the average value was determined.

Kinetic modeling of drug release

The dissolution profile of all the formulations was fitted in to zero-order, first-order, and Higuchi and Korsmeyer-peppas models to ascertain the kinetic modeling of drug release.[18-21]

RESULTS AND DISCUSSION

Fast Dissolving tablets of Moxifloxacin.HClwere prepared and optimized by 3^2 factorial design in order to select the best combination of different Superdisintegrants, Crospovidone, Croscarmellose sodium and also to achieve the desired rapid release of drug from the dosage form(by Disintegrating quickly). The two factorial parameters involved in the development of formulations are, quantity of Crospovidone&Croscarmellose sodium as independent variables (X_1, X_2), and *In vitro* dissolution parameters such as $t_{50\%}$, $t_{90\%}$, Wetting time and Disintegrating Time as dependent variables Totally nine formulations were prepared using 3 levels of 2 factors and all the formulations containing 400 mg of Moxifloxacin. HClwere prepared as a Fast Dissolving tablet dosage form by Direct Compression technique as per the formulae given in Table 2.

All the prepared tablets were evaluated for different post compression parameters, drug content, mean hardness, friability, mean thickness, Weight variation as per official methods and results are given in Table 3. The hardness of tablets was in the range of **4.610±0.15-4.845±0.15 Kg/cm².** Weight loss in the friability test was not more than **0.78%**. Drug content of prepared tablets was within **acceptance range only**. The Wetting Time of tablets was in the range of **43.05±1.3-83.75±1.6 sec.** The Disintegration Time of tablets was in the range of **62.09±1.5-125.90±1.6 sec.** Results for all Post-compression parameters were tabulated or shown in Table 3. *In-vitro* Dissolution studies were performed for prepared tablets using Phosphate buffer pH 6.8 as a dissolution media at 50 rpm and temperature 37±0.5°C. The *In-vitro* dissolution profiles of tablets are shown in Figure 1-4 (Kinetic Plots), Wetting Time Chart, Disintegration Time charts were shown in Figure 5-6. The dissolution parameters are given in Table 4. Cumulative % Drug release of Factorial Design Formulations F_1-F_9 at 30 mins were found to be in the range of **98.75-99.65 %**. From the result it reveals that the release rate was higher for formulations containing High level of Crospovidone/Croscarmellose sodium compared with other Formulations containing Lower level, due to High concentration of Superdisintegrant in combination, shows various disintegration mechanism such as wicking and swelling etc more compared with lower concentration and alone, drug may release rapidly and shows improved bioavailability. Excess of Superdisintegrant also prone to Friable. Therefore, required release of drug can be obtained by manipulating the com-

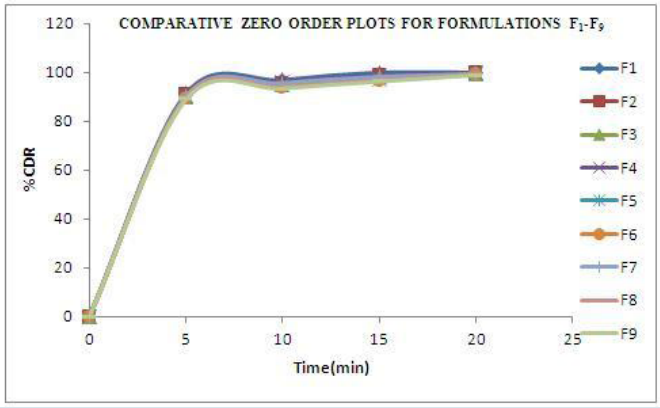

Figure 1: Comparative Zero Order Plots.

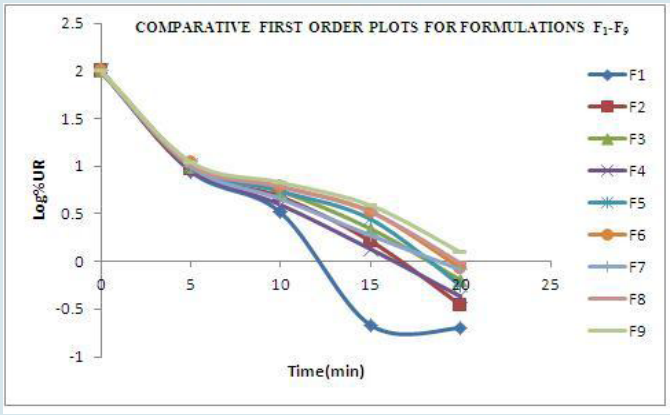

Figure 2: Comparative First Order Plots.

position of Crospovidone and Croscarmellose sodium.

Variation was observed in the Wetting time,Disintegrating time, $t_{50\%}$and $t_{90\%}$ due to formulation variables. Formulation F_5 containing 45 mg of Crospovidone, 45 mg of Croscarmellose sodium showed promising dissolution parameter (**Wetting time = 50.66±1.5**sec,**Disintegrating time = 73.85±1.5**sec, **$t50_{\%}$ = 2.968** min, **$t_{90\%}$ = 9.864** min). The difference in burst effect of the initial time is a result of the difference in the Concentration of Superdisintegrantsmixtures. This reveals that increasedconcentration of superdisintegrants resulted in a corresponding decrease in the Wetting Time, which might be due to the result of wicking and other possible disintegrating mechanisms. Disintegration time is directly proportional to wetting time.

The *In -vitro* dissolution data of Moxifloxacin.HClFast Dissolving formulations was subjected to goodness of fit test by linear regression anal-

Table 1: Experimental Design Layout

Formulation Code	X_1	X_2
F_1	1	1
F_2	1	0
F_3	1	-1
F_4	0	1
F_5	0	0
F_6	0	-1
F_7	-1	1
F_8	-1	0
F_9	-1	-1
C_1	-0.5	-0.5
C_2	+0.5	+0.5

Table 2: Formulae for the Preparation of Moxifloxacin.HCl Fast Dissolving Tablets as Per Experimental Design

Name of Ingredients	Quantity of Ingredients per each Tablet (mg)								
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Moxifloxacin. HCl	400	400	400	400	400	400	400	400	400
Emcompress	59	74	89	74	89	104	89	104	119
Crospovidone	60	60	60	45	45	45	30	30	30
Croscarmellose sodium	60	45	30	60	45	30	60	45	30
Magnesium Stearate	8	8	8	8	8	8	8	8	8
Talc	8	8	8	8	8	8	8	8	8
Aspartame	5	5	5	5	5	5	5	5	5
Total Weight	600	600	600	600	600	600	600	600	600

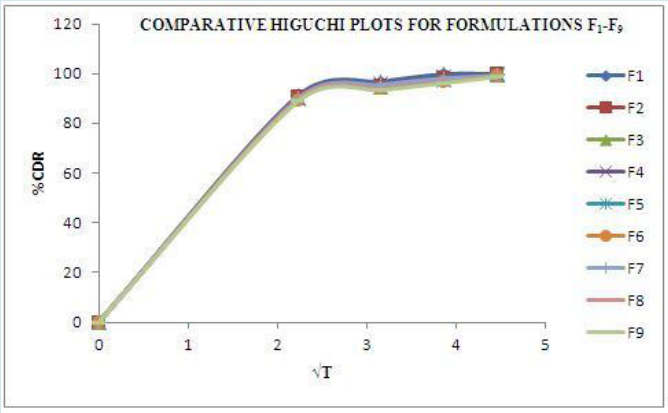

Figure 3: Comparative Higuchi Plots.

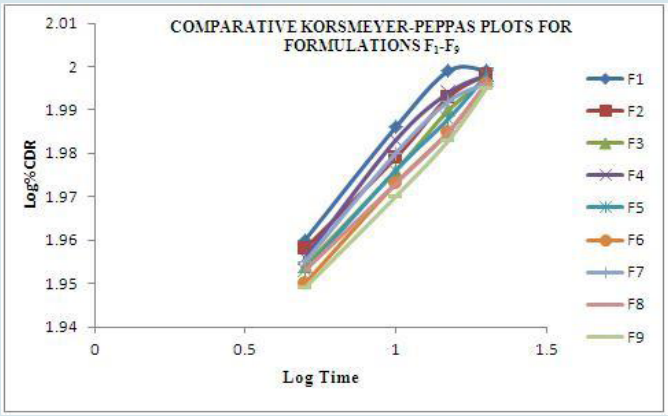

Figure 4: Comparative Korsemeyer-Peppas Plots.

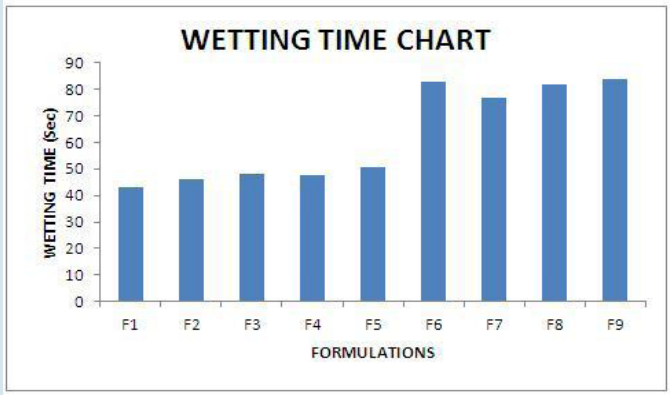

Figure 5: Wetting Time Chart.

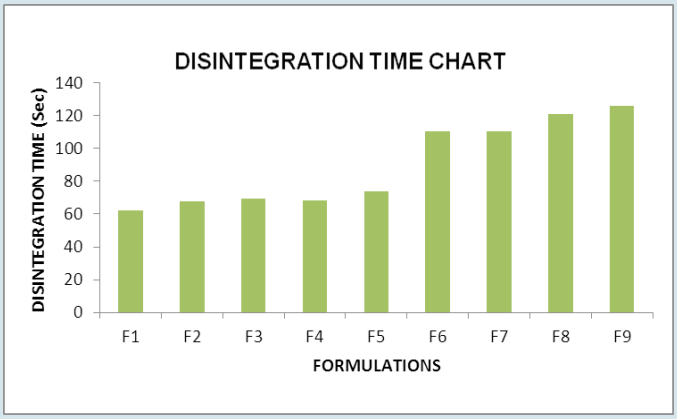

Figure 6: Disintegration Time Chart.

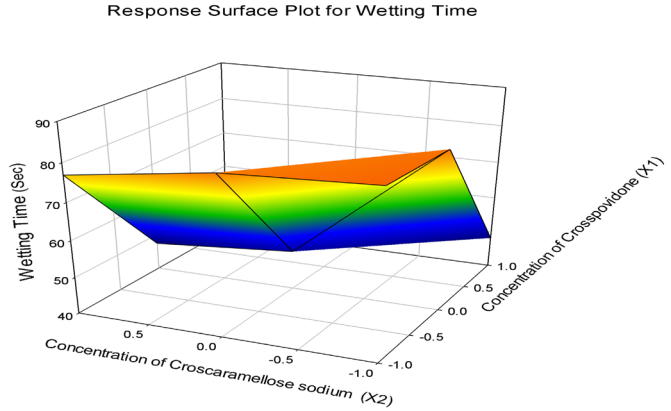

Figure 7: Response Surface Plot for Wetting Time.

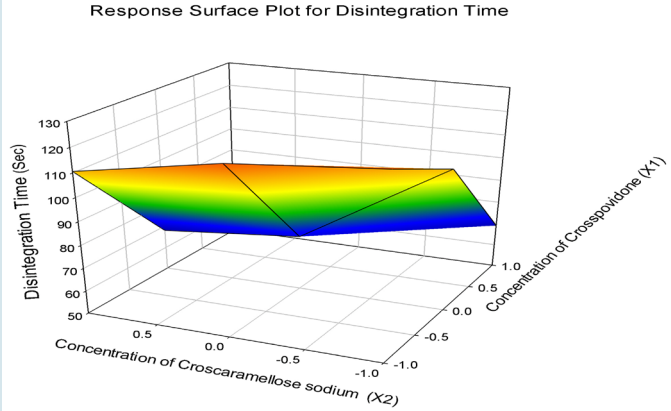

Figure 8: Response Surface Plot for Disintegration Time.

Table 3: Post-Compression Parameters for the Formulations

Formulation Code	Hardness (kg/cm2)	Thickness (mm)	Friability (%)	% Weight Variation	Drug Content (%)	Wetting Time(sec)	Disintegration Time (sec)
F_1	4.845±0.15	3.739±0.15	0.776±0.12	Pass	99.58±0.25	43.05±1.3	62.09±1.5
F_2	4.805±0.14	3.784±0.14	0.712±0.13	Pass	99.98±0.30	46.22±1.4	67.88±1.6
F_3	4.745±0.15	3.725±0.16	0.704±0.1	Pass	98.77±0.50	48.26±1.6	69.14±1.8
F_4	4.735±0.13	3.830±0.10	0.764±0.12	Pass	99.805±.40	47.44±1.4	68.05±1.4
F_5	4.690±0.14	3.890±0.11	0.699±0.13	Pass	100.205±0.90	50.66±1.5	73.85±1.5
F_6	4.610±0.15	3.834±0.12	0.692±0.05	Pass	98.995±0.70	82.72±1.7	110.51±1.7
F_7	**4.712±0.16**	**3.817±0.10**	**0.753±0.13**	**Pass**	**98.996±0.25**	**76.95±1.3**	**110.58±1.4**
F_8	**4.675±0.14**	**3.872±0.12**	**0.689±0.132**	**Pass**	**99.395±0.30**	**82.08±1.5**	**120.84±1.5**
F_9	**4.615±0.16**	**3.810±0.11**	**0.681±0.140**	Pass	98.185±0.50	83.75±1.6	125.90±1.7

Table 4: Regression Analysis Data of 3^2 Factorial Design Formulations of Moxifloxacin.HCl Fast Dissolving Tablets

Formulation Code	KINETIC PARAMETERS											
	ZERO ORDER			FIRST ORDER			HIGUCHI			KORSMEYER-PEPPAS		
	a	b	r	a	b	r	a	b	r	a	b	r
F_1	35.860	4.164	0.757	1.821	0.140	0.971	15.109	22.699	0.913	1.914	0.069	0.976
F_2	35.388	4.139	0.760	1.815	0.113	0.981	14.894	22.515	0.914	1.909	0.070	0.998
F_3	35.038	4.130	0.762	1.786	0.101	0.975	14.690	22.429	0.916	1.903	0.073	0.999
F_4	35.412	4.150	0.760	1.787	0.112	0.982	14.857	22.577	0.915	1.907	0.073	0.987
F_5	34.936	4.126	0.763	1.801	0.101	0.972	14.639	22.396	0.916	1.902	0.073	1.000
F_6	34.586	4.117	0.766	1.786	0.093	0.967	14.434	22.310	0.917	1.896	0.076	0.999
F_7	35.308	4.127	0.760	1.746	0.098	0.968	14.846	22.459	0.914	1.907	0.071	0.992
F_8	34.834	4.103	0.762	1.766	0.091	0.963	14.629	22.276	0.915	1.902	0.071	0.999
F_9	34.484	4.094	0.765	1.764	0.085	0.958	14.425	22.191	0.917	1.896	0.074	0.998

F_1 to F_9 are factorial formulations, r-correlation coefficient, a-Intercept, b-Slope

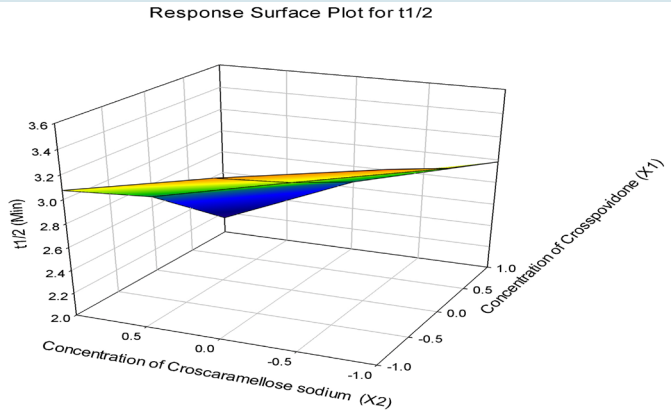

Figure 9: Response Surface Plot for t50%.

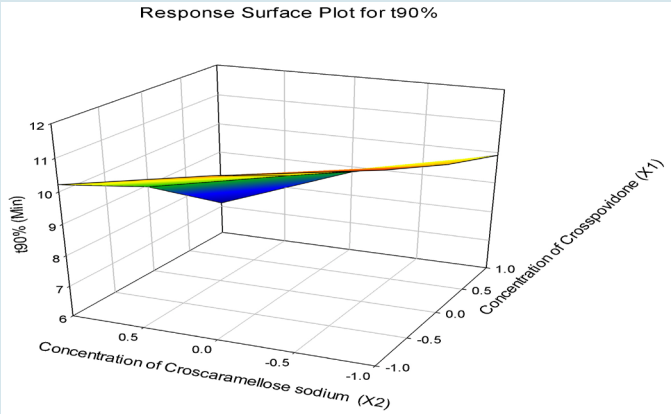

Figure 10: Response Surface Plot for t90%.

Table 5: Dissolution Parameters of Moxifloxacin.HCl Fast Dissolving Tablets 3^2 Full Factorial Design Batches

FORMULATION CODE	KINETIC PARAMETERS				
	$t_{1/2}$	$t_{10\%}$	$t_{90\%}$	WT(Sec)	DT(Sec)
F_1	2.146	0.326	7.131	43.05	62.09
F_2	2.655	0.404	8.824	46.22	67.88
F_3	2.982	0.453	9.910	48.26	69.14
F_4	2.691	0.409	8.943	47.44	68.05
F_5	2.968	0.451	9.864	50.65	73.845
F_6	3.232	0.491	10.741	82.71	`110.51
F_7	3.075	0.467	10.219	76.94	110.58
F_8	3.321	0.505	11.034	82.08	120.84
F_9	3.530	0.537	11.731	83.75	125.90

ysis according to zero order and first order kinetic equations, Higuchi's and Korsmeyer-Peppas models to assess the mechanism of drug release. The results of linear regression analysis including regression coefficients are summarized in Table 4. It was observed from the above that dissolution of all the tablets followed First order kinetics with co-efficient of determination (R^2) values in the range of **0.958-0.982**. The values of r of factorial formulations for Higuchi's equation was found to be in the range of **0.913-0.917**, which shows that the dissolution data fitted well to Higuchi's square root of time equation confirming the release followed diffusion mechanism. Kinetic data also treated for Peppas equation, the slope (n) values ranges from **1.896-1.914** that shows Fickian diffusion mechanism. Polynomial equations were derived for wetting time, Disintegrating time, $t_{50\%}$ and $t_{90\%}$ values by backward stepwise linear regression analysisusing **PCP Disso** software and Response surface plots were constructed using **SIGMAPLOT V13**software. The Response surface plotswere shown in Figure 7-10 for Wetting time,Disintegrating time, $t_{50\%\text{ and }}$ $t_{90\%}$ using X_1 and X_2 on both the axes respectively. The dissolution data (Kinetic parameters) of factorial formulations F_1 to F_9 are shown in Table 5.

Polynomial equation for 3^2 full factorial designs is given in Equation

$Y= b_0+b_1 X_1+b_2 X_2+b_{12} X_1X_2+b_{11} X_1^2+b_{22} X_2^2\ldots$

Where, Y is dependent variable, b_0 arithmetic mean response of nine batches, and b_1 estimated co-efficient for factor X_1. The main effects (X_1 and X_2) represent the average result of changing one factor at a time from its low to high value. The interaction term (X_1X_2) shows how the response changes when two factors are simultaneously changed. The polynomial terms (X_1^2 and X_2^2) are included to investigate non-linearity. Validity of derived equations was verified by preparing Two Check point Formulations of Intermediate concentration (C_1, C_2).

The equations for Wetting time, Disintegrating time, $t_{50\%}$ and $t_{90\%}$ developed as follows,

$Y_1= 62.344-17.54X_1-7.882X_2+0.400X_1X_2+3.12 X_1^2+4.042X_2^2$**(for Wetting time)**

$Y_2= 89.87-26.37X_1-10.805X_2+2.068 X_1X_2+8.60 X_1^2+3.52 X_2^2$**(for Disintegration time)**

$Y_3= 2.96-0.357X_1-0.305X_2-0.095 X_1X_2-0.012 X_1^2-0.039 X_2^2$**(for $t_{50\%}$)**

$Y_4= 9.822-1.187X_1-1.015X_2-0.317 X_1X_2-0.042 X_1^2-0.128 X_2^2$**(for $t_{90\%}$)**

The positive sign for co-efficient of X_1 in Y_1, Y_2, Y_3 and Y_4 equations indicates that, as the concentration of Crospovidonedecreases, Wetting time, Disintegrating time, $t_{50\%}$and $t_{90\%}$ value increases. In other words the data demonstrate that both X_1 (Quantity of Crospovidone) and X_2 (Quantity of Croscarmellose sodium) affect the time required for drug release (Wetting time, Disintegrating time, $t_{50\%}$and $t_{90\%}$). From the results it can be concluded that, and increase in the Quantity of the Superdisintegrant leads to decrease in Disintegration time of the Dosage form and drug release pattern may be changed by appropriate selection of the X_1 and X_2 levels. The Dissolution parameters for predicted from the polynomial equations derived and those actual observed from experimental results are summarized in Table 6. The closeness of Predicted and Observed values for Wetting time,Disintegrating time,$t_{50\%}$and $t_{90\%}$ indicates validity of derived equations for dependent variables. The Response sur-

Table 6: Dissolution Parameters for Predicted and Observed Values for Check Point Formulations

FORMULATION CODE	PREDICTED VALUE				ACTUAL OBSERVED VALUE			
	WT(Sec)	DT(Sec)	$t_{50\%}$ (min)	$t_{90\%}$ (min)	WT(Sec)	DT(Sec)	$t_{50\%}$ (min)	$t_{90\%}$ (min)
C_1	76.95	112.0045	3.232	10.8013	77.12	115.21	3.29	10.94
C_2	51.52	74.83	2.57	8.60	50.38	75.39	2.68	8.54

face Plots were presented to show the effects of X_1 and X_2 on Wetting time, Disintegrating time, $t50_{\%}$ and $t_{90\%}$. The final best (Optimized) formulation (F_5) is compared with marketed product (**AVELOX-400**) shows similarity factor (f_2) 68.88, difference factor (f_1) 3.35 (There is no significant difference in drug release because t_{cal} is<0.05).

CONCLUSION

The present research work envisages the applicability of Superdisintegrants such as Crospovidone and Croscarmellose sodium in the design and development of Fast Dissolving tablet formulations of Moxifloxacin.HClutilizing the 3^2 factorial design. From the results it was clearly understand that as the concentration of Superdisintegrant increases the release rate of drug was RAPID (Improved Solubility) and both of these Superdisintegrants can be used in combination since do not interact with the drug which may be more helpful in achieving the desired fast Dissolving of the dosage form for rapid action and improved Bioavailability. The optimized formulation followed Higuchi's kinetics while the drug release mechanism was found to be Fickian Diffusion, first order release type. On the basis of evaluation parameters, the optimized formulation F_5 may be used for the effective management of acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, community acquired pneumonia, complicated and uncomplicated skin and skin structure infections, and complicated intra-abdominal infections.This may improve the patient compliance by showing rapid action via disintegration without difficult in swallowing and side effects which will ultimately improve the therapeutic outcome. We could be able to minimize the per oral cost of the Formulation.

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CONFLICT OF INTEREST

None

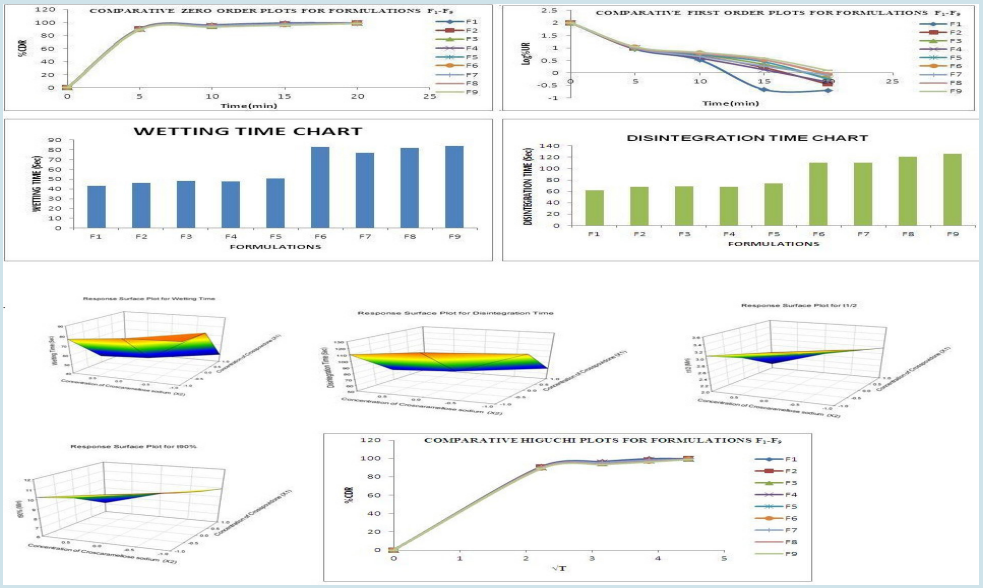
ABBREVIATION USED

ODT: Oral Disintegrating Tablet; DNA: Deoxyribo Nucleic Acid; Kg: KiloGram; Cm: CentiMeter; %: Percentage; mg: milli gram; ml: milli litre; %CDR: Percentage Cumulative Drug Release; BCS: Biopharmaceutical Classification; UR: Un Released; Min: Minute; °C: Degree Centigrade; mm: milli meter.

REFERENCES

1. Kavitha K, KumuthaSubramaniam B, Santhi K, Dhanaraj SA, Kumar MR. Potential Drug Candidates for Fast Dissolving Drug Delivery-A Review. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2013;4(4):1510-26.
2. Gunda RK, Kumar JS, Jayakumari S, Vijayalakshmi A, Satyanarayana V. Formulation Development and Evaluation of Risperidone Fast Dissolving Tablets. Journal of Pharmacy Research Vol. 2016;10(9):579-88.
3. Kumar V.K, Ajaykumar B. Formulation and evaluation of rapid disintegration tablets of moxifloxacin HCl. Der Pharmacia Lettre, 2013;5(1):238-50.
4. Reddy LH, Ghosh B. Fast dissolving drug delivery systems: A review of the literature. Indian Journal Pharmaceutical Sciences. 2002;64:331.
5. Gunda RK, Kumar JS, Babu CA, Anjaneyulu MV. Formulation development and evaluation of lamotrigine sustained release tablets using 32 factorial design. International Journal of Pharmaceutical Sciences and Research, 2015;6(4):1746.
6. Shende M.A, Marathe R.P, Khetmalas S.B, Dhabale P. N. Studies on development of Sustained release Diltiazem hydrochloride matrices through jackfruit mucilage. International Journal of pharmacy and pharmaceutical sciences,2014;6(7):72-8.
7. Schwartz BJ, Connor RE. Optimization technique in pharmaceutical formulations and processing. J Drugs and Pharm Sciin Modern Pharmaceutics.1996;72(3):727-54.
8. Kumar R.G, Kumar S.J.N. Formulation Development and Evaluation of Zidovudine Sustained Release Tablets Using 32 Factorial Design, Der Pharmacia Sinica, 2015;6(6):59-67.
9. Kumar S.J.N, Gunji S.B, Kumar V.C.B and Kumar R.G, Formulation Development and Evaluation of Metoprolol Succinate Sustained Release Tablets Using 32 Factorial Design, Der Pharmacia Lettre, 2015;7(7):148-57.
10. 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;72(5):599. https://doi.org/10.4103/0250-474X.78527; PMid:21694992 PMCid:PMC3116305.
11. Gunda RK. Formulation development and evaluation of rosiglitazone maleate sustained release tablets using 32 factorial design. IJPTR. 2015;8:713-24.
12. Raghavendra kumar gu, kumar js, satyanarayana v, swarupa rani g, satya prasad b. Formulation development and evaluation of clopidogrel fast dissolving tablets. Iranian journal of pharmaceutical sciences. 2016;12(2):61-74
13. Raghavendra Kumar Gunda, J. N. Suresh Kumar, Kumar B.C, SatyanarayanaV, PrashantN.K. Design, Formulation and Evaluation of Atenolol Gastro Retentive Floating Tablets. Asian Journal of Pharmaceutics 2015; 9 (4) (Suppl) S34-S42.
14. Ramji Anil Kumar Arza, B. Vijaya Kumar. Development and evaluation of gastroretentive floating matrix tablets of moxifloxacin HCl. Der Pharmacia Lettre, 2016, 8 (10):140-149.
15. Gunda RK, Kumar JS, Satyanarayana V, Batta S, Harika CM. Formulation Development and Evaluation of Carbamazepine Fast Dissolving Tablets. Journal of Pharmacy Research. 2016;10(5):216-25.
16. Rao NG, Kulkarni U. Development of Carbamazepine fast dissolving tablets: Effect of functionality of Hydrophilic carriers on solid dispersion technique. Asian. J. Pharma. Clinical Res. 2010;3(2).
17. Hardenia SS, Darwhekar GN, AnuHardenia SS. Designing and Pharmaceutical Evaluation of Fast Dissolving Tablet of Fexofenadine Using Coprocessed Superdisintegrants. International Journal of Pharmaceutical Sciences and Research. 2014;5(7):3018-30.
18. Kumar R.G, Kumar S.J, Satyanarayana V, Ramananjaneyulu K.V, satyprasad B. Formulation Development and Evaluation of Carvedilol Phopsphate Gastro Retentive Floating Tablets. International Research Journal of Pharmacy. 2016;7(1):44-51.
19. Notari RE. Bio pharmaceutics and clinical pharmacokinetics. 4th ed. New York: Marcel Dekker Inc; 1987; 6-21.
20. Higuchi T. Mechanism of sustained-action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. Journal of pharmaceutical sciences. 1963 Dec 1;52(12):1145-9.https://doi.org/10.1002/jps.2600521210; PMid:14088963.
21. Peppas NA. Analysis of fickian and non-fickian drug release from polymers Pharmaceutical Acta Helvetiae . 1985;60:110-1.PMid:4011621.

PICTORIAL ABSTRACT



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