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Design, Optimization and Evaluation of Piroxicam Fast Dissolving Tablets Employing Modified Starch by 2^3 Factorial Design

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ABSTRACT

Fast dissolving tablet have potential advantages over conventional dosage forms, which has helped patient compliance, convenience, bioavailability and rapid onset of action. These are very good for drug delivery over geriatric and pediatric patients. They have significant advantages of solid and liquid dosage forms, because when they are in solid form and when transformed into liquid form and within few seconds after it is consumed. With new technologies for it formulation many commercial products are available in the market for the patients. So FDT have awful scope for being the delivery system. Therefore in the present investigation, starch based superdisintegrant was prepared and evaluated for its application in the design of fast dissolving dosage forms of piroxicam.

Keywords: Fast Dissolving Tablets, Superdisintegrant, Modified Starch, Piroxicam.

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INTRODUCTION:

Fast dissolving tablets are solid dosage forms containing medicinal substances which disintegrate rapidly, usually within few seconds when placed upon tongue requiring no additional water, to facilitate swallowing. Various techniques can be used to formulate fast dissolving tablets. Direct compression method, one of most oldest and convenient method of formulating tablets. Direct compression method needs only the cheaper excipients. Therefore the dosage forms which were formulated by direct compression method will be cheaper than the dosage forms formulated by other methods. The aim of the work was to formulate and evaluate fast dissolving tablets of piroxicam employing modified starch as a superdisintegrant for rapid dissolution and absorption of drugs, which may produce the rapid onset of action of drug.

Optimization technique

Optimization techniques facilitate the clear understanding and can be ability to explore and define ranges for formulation and processing factors with a careful approach for the selection of several experimental and manufacturing steps for a given product.

The present study deals with the investigation for optimization of piroxicam fast dissolving tablets employing modified starch, crosscaramallose sodium, and crospovidone as superdisintegrants. A 2^3 factorial design was applied to investigate the main and interaction effects of the three formulation variables that is, modified starch (A), crosscaramallose sodium (B) and crosprovidone (C) in each case to find the formulation with less disintegration time and more dissolution efficiency in 5 min and permit and arbitrary detection of tablets with immediate release of drug within ten minutes.

MATERIALS & METHODS

1. Piroxicam (Yarrow chemicals, Mumbai).
2. Modified starch (Synthesized in laboratory).
3. Croscarmellose sodium (Yarrow chemicals, Mumbai).
4. Crospovidone (Yarrow chemicals, Mumbai)
5. Mannitol (Yarrow chemicals, Mumbai)
6. Microcrystalline cellulose (Quligens fine chemicals, Mumbai).

7. Talc (Molychem, Mumbai)
8. Magnesium stearate (Molychem, Mumbai)

Preparation of modified starch acid:

Initially10 grams of glutaric acid was dissolved in distilled water and the pH was adjusted to 3.5 using 10M sodium hydroxide and finally made up to 25 ml. To the above mixture 25 grams potato starch was added and conditioned for 16 hrs at room temperature, later the product was kept in oven at 60^{0}C for 6 hrs, the mass was washed to remove un reacted glutaric acid. After washing the product was dried at 60^{0}C. The product obtained was ground and sieved (# 100).

Preparation of Piroxicam Fast Dissolving Tablets:

The tablets were prepared by direct compression method. The composition of formulations of piroxicam fast dissolving tablets is shown in table no 1. For uniformity in particle size each ingredient was passed through # 100 mesh sized screen before mixing. Modified starch, croscarmellosesodium, crosprovidone, mannitol, microcrystalline cellulose, were accurately weighed and mixed using motor and pestle, and then added to piroxicam. Finally talc and magnesium stearate were added to the powder. Finally mixed blend was compressed by using eight station rotator press (Shakthi Machinineries Pvt. Ltd., Ahmadabad).

Evaluation of Piroxicam Fast Dissolving Tablets:

Hardness: [1].

The hardness of the tablet is the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring and expressed in kg/cm^2.

Uniformity of Weight: [1].

Weight variation test was done with 20 tablets. It is the individual variation of tablet weight form the average weight of 20 tablets.

Average weight of tablet	% Deviations
80 mg or less	±10
More than 80 mg or less than 250 mg	±7.5
More than 250 mg	± 5

Friability: [1].

The friability of tablets was measured using a Roche friabilator. Tablets were rotated at 25 rpm for 4 minutes or to 100 revolutions. The tablets were then reweighed after removal of fines and the percentage of weight of weight loss was calculated.

$$F = \frac{W_{(initial)} - W_{(final)}}{W_{(initial)}} x\ 100$$

Drug Content Uniformity: [2].

For content uniformity test, ten tablets were weighed and powdered. A quantity of powder equivalent to 100 mg of piroxicam was extracted into 0.1N hydrochloric acid buffer and filtered. The piroxicam content was determined by measuring the absorbance spectrophotometrically at 333 nm after appropriate dilution with 0.1N hydrochloric acid buffer. The drug content was calculated using the standard calibration curve. The mean percentage drug content was calculated as an average of three determinations.

Wetting Time: [3].

The wetting time of the tablet was noted as the time taken by the water to reach the upper surface of the tablet, when the tablet is placed in water. The wetting time of the tablets was measured using a very simple process. Five circular tissue papers were placed in a petridish with a 10 cm diameter. Ten milliliters of water containing soluble dye (Amaranth) was added to the petridis and a fast dissolving tablet was carefully placed on the surface of paper. The time taken by to tablet to become red is noted as wetting time.

Water Absorption Ratio: [4].

Initially the fast dissolving tablet was weighed. Then tablet was put on the tissue paper which was folded twice a small petridish a containing 6 ml of water, and allowed to wet completely. The wetted tablet was then weighted. Water absorption ratio, R was determined using following equation.

$$R = \frac{100(W_1 - W_2)}{W_1}$$

Where

W_1 = weight of tablet after water absorption

W_2= weight of tablet before water absorption

***In vitro* Disintegration Time:** [5].

Disintegration time for FDTs was determined using USP disintegration apparatus with pH 0.1N hydrochloric acid buffer. The volume of medium was 900 ml and temperature was 37±0.2^{0}C. The time in seconds taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured.

***In Vitro* Dissolution Rate Studies: [5].**

The *in vitro* dissolution rate study of piroxicam fast dissolving tablets was performed using 8 station dissolution test apparatus (Electro lab TDT- 08L) fitted with paddles (50 ppm) at 37 ± 0.5^0 C, using pH 0.1N hydrochloric acid (900 ml) as a dissolution media. At the predetermined time intervals 5 ml sample was withdrawn, filtered through 0.45 µ membrane filter, diluted and assayed at 333 nm using a Analytical technology Elico SL 191 UV/Visible Double beam spectrophotometer. Cumulative percentage drug dissolved was calculated using standard absorbance from the calibration curve. All the dissolution experiments were conducted in triplicate (n=3).

Optimization:

The percentages of modified starch (A), croscarmellose sodium (B) and crospovidone (C) were selected as independent variables. The dissolution efficiency in 5 minutes was selected as dependent variable. The resulting data was fitted into Stat Ease, Inc. (Minneapolis, MN) Design Expert 11 Version software and analyzed statistically using analysis of Variance (ANOVA). The data were also subjected to 3-D response surface methodology to determine the influence of modified starch, croscarmellose sodium, crospovidone and interactions between them on dependent variable.

Comparison of Optimized formula with the Marketed Sample:

The optimized formula will be compared with the marketed formula for all its physical properties and dissolution

parameters. The marketed sample available in the local market was

MOBICAM-DT

B.NO. B670823

MFG. AUG.2017 Exp. JUL.20

CIPLA

Mfg. by. Cipla. LTD.

Village tanda mallu, Kosing.road

Ram Nagar (Dist)

Table 1: Formulation of Piroxicam Fast Dissolving Tablets Employing Modified starch

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8
Piroxicam	20	20	20	20	20	20	20	20
Modified Starch	-	10	-	10	-	10	-	10
Croscarmellose sodium	-	-	10	10	-	-	10	10
Crospovidone	-	-	-	-	10	10	10	10
Mannitol	72	62	62	52	62	52	52	42
Micro crystalline cellulose	100	100	100	100	100	100	100	100
Talc	4	4	4	4	4	4	4	4
Magnesium stearate	4	4	4	4	4	4	4	4
Total weight	200	200	200	200	200	200	200	200

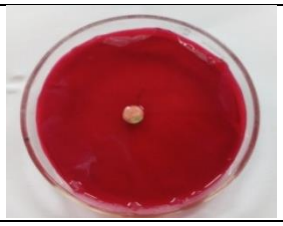
Table 2: Physical properties: Hardness, Friability, Drug Content, Wetting Time, Water Absorption Ratio of Piroxicam Fast Dissolving Tablets.

Formul-ation code	Hardness (Kg/Cm^2) ±S.D	Friability (%)±S.D	Drug Content± S.D	Disintegration Time (S)±S.D	Wetting Time (sec)±S.D	Water Absorption Ratio(%)±S.D
F1	3.7±0.01	0.12±0.013	19.85±0.1	10818±0.6	285±0.2	0.44±0.1
F2	3.7±0.03	0.13±0.015	19.21±0.2	53±0.5	22±0.12	1.89±0.18
F3	3.7±0.01	0.14±0.012	19.16±0.2	210±0.02	120 ±0.09	1.77±0.16
F4	3.7±0.04	0.12±0.014	19.56±0.16	325±0.02	176±0.02	1.16±0.15
F5	3.8±0.03	0.14±0.012	19.83±0.26	380±0.01	158±0.21	1.77±0.21
F6	3.9±0.01	0.15±0.012	19.34±0.12	323±0.02	42±0.09	1.22±0.12
F7	3.8±0.02	0.14±0.014	19.65±0.7	102±0.01	33±0.13	1.15±0.15
F8	3.7±0.04	0.12±0.013	19.27±0.11	132± 0.02	26±0.1	1.55±0.27

*SD standard deviation from mean, n=3, mean±SD.

Fig: 1(a) Wetting Times of Piroxicam Fast Dissolving Tablets Formulated Employing Modified Starch - (A Novel Superdisintegrant)

F1 Piroxicam Fast Dissolving Tablets



At T=0 sec **At T=285 sec**

F2 Piroxicam Fast Dissolving Tablets

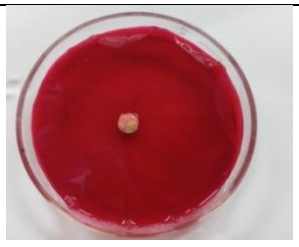


Fig: 1(b) Wetting Times of Piroxicam Fast Dissolving Tablets Formulated Employing Modified Starch - (A Novel Superdisintegrant)

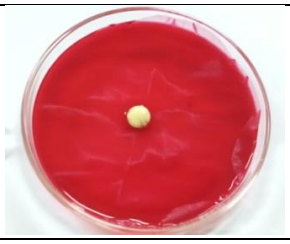
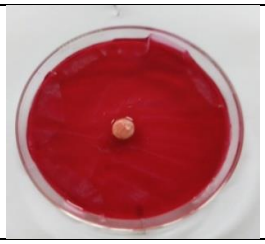
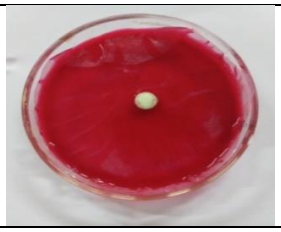
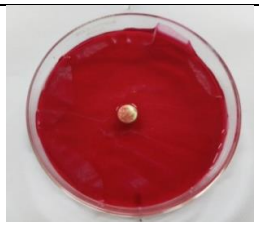
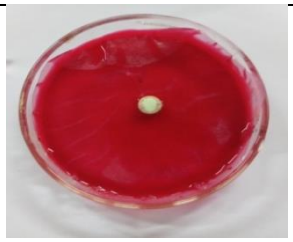
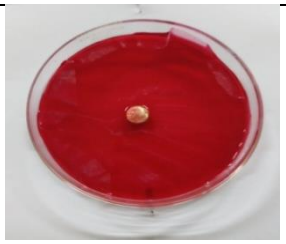
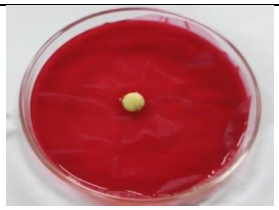
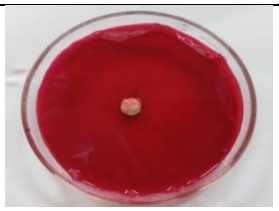
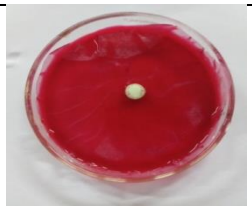
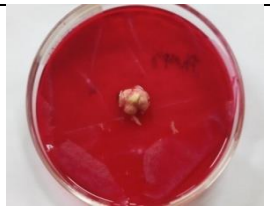
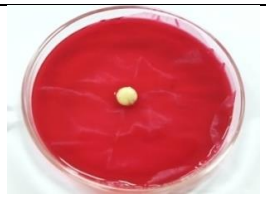
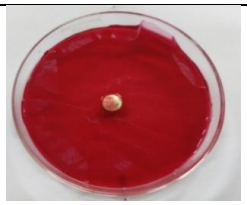
At T=0 sec	At T=22 sec
F3 Piroxicam Fast Dissolving Tablets	
	
At T=0 sec	**At T=120 sec**
F4 Piroxicam Fast Dissolving Tablets	
	
At T=0 sec	**At T=176 sec**
F5 Piroxicam Fast Dissolving Tablets	
	
At T=0 sec	**At T=158 sec**
F6 Piroxicam Fast Dissolving Tablets	
	
At T=0 sec	**At T=42 sec**
F7 Piroxicam Fast Dissolving Tablets	
	
At T=0	**At T=33 sec**
F8 Piroxicam Fast Dissolving Tablets	
	
At T=0	**At T=26 sec**

Table: 3. Piroxicam Dissolution Data of Fast Dissolving Tablets Employing Modified Starch

Piroxicam Percent Dissolved from Fast Dissolving Tablets Employing Modified Starch

Time (Min)	F1	F2	F3	F4	F5	F6	F7	F8
5	5.1± 0.1	85.12±0.2	46.77±0.3	39.5±0.3	44.21±0.2	40.11± 1.3	65.02±0.6	74.62±2.3
10	7.3±2.1	99.89±0.4	50.71±2.1	39.85±2.1	47.12±1.3	41.3±2.1	70.37±1.2	84.09±0.2
15	11.2±2.3	-	52.9±3.2	46.79±1.3	50.32±0.5	44.7±1.3	73.48±0.6	86.36±3.1
30	16.5±0.3	-	55.84±0.5	45 ±2.3	51.77±0.6	47.12±2.3	84.91±0.5	93.37±0.6
45	20.6±0.5	-	61.65±0.6	56.36±2.6	53.25±0.3	65.95±0.2	93.54±0.4	99.44±1.3
60	22.4±0.2	-	68.92±0.5	61.86±3.1	57.12±0.6	76.51±0.6	99.62±1.5	-

*SD standard deviation from mean, n=3, mean±SD.

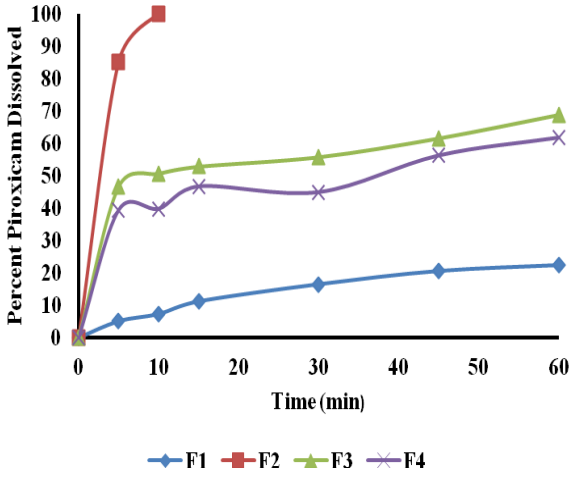


Fig. 2: Dissolution Profiles of Piroxicam Fast Dissolving Tablets Employing Modified Starch (F1 to F4)

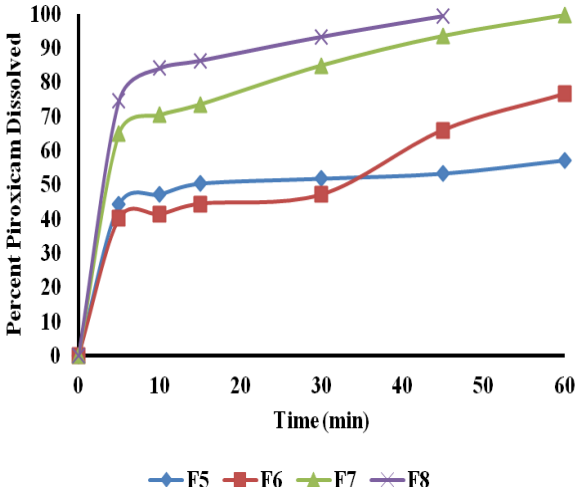


Fig. 3: Dissolution Profiles of Piroxicam Fast Dissolving Tablets Employing Modified Starch. (F5 to F8)

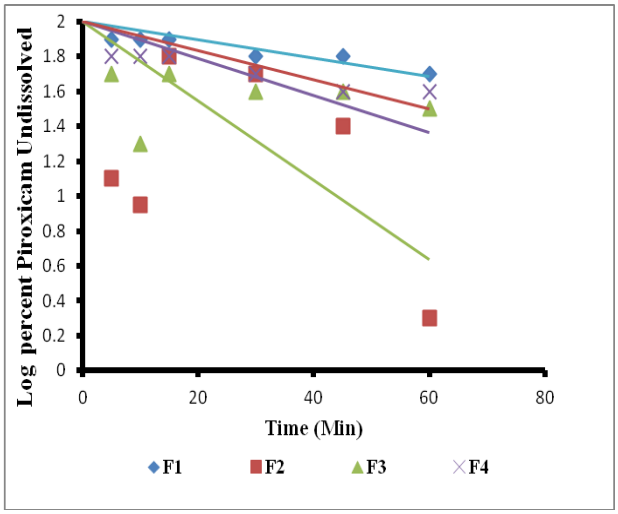


Fig 4: Log Time Vs Log Percent Undissolved Piroxicam Fast Dissolving Tablets Employing Modified Starch Prepared By Direct Compression Method (F1 to F4)

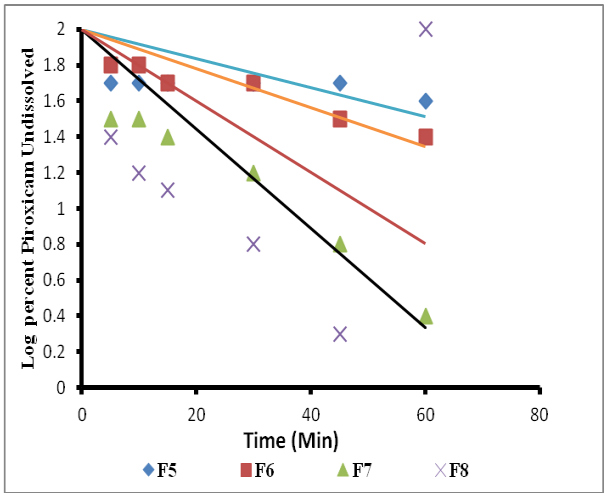


Fig 5: Log Time Vs Log Percent Undissolved Piroxicam Fast Dissolving Tablets Employing Modified Starch Prepared by Direct Compression Method (F5 to F8)

Table 4: Dissolution Parameters of Piroxicam Fast Dissolving Tablets Formulated Employing Modified Starch

Parameter	F1	F2	F3	F4	F5	F6	F7	F8
PD_5	5.1±0.1	85.12±0.2	46.77±0.3	39.50±0.3	44.21±0.2	40.11±1	74.62±0.3	65.02±0.6
DE_5 (%)	3.6±0.01	83.3±0.03	43.4±0.02	37.2±0.01	41.9±0.02	37±0.03	72.5±0.04	62.6±0.05
Increase in DE_5 (%) No. of folds	-	23.13	12.05	10.33	11.63	10.27	20.13	17.38
K_1 (min^{-1})	0.01±0.01	0.06±0.02	0.18±0.12	7.6±0.03	2.3±0.05	0.01±0.05	0.04±0.2	0.05±0.01
Increase in K_1 (min^{-1}) No. of folds	-	6	18	760	230	1	4	5

*SD standard deviation from mean, n=3, mean±SD, PD_5-Percent dissolved in 5 min., DE_5%-Dissolution efficiency in 5 min., K_1 =First order rate constant

RESULTS AND DISCUSSION

Fast dissolving tablets each containing 20 mg of piroxicam could be prepared by employing modified starch and other known superdisintegrants, croscarmellose sodium and crosprovidone by direct compression method. Hardness of the tablets was in range of 3.7-3.9 kg/sq.cm. It indicates good strength with a capability to resist physical and pre functionary stress condition during handling. Weight loss on the friability test was less than 0.16% in all cases. All the fast dissolving tablets prepared containg piroxicam with in 100±5% of the labeled claim. As such the prepared tablets were of good quality with respect to drug content, hardness and friability. The disintegration time of all formulated tablets was found to be in the range of 53±0.05 to 10818±0.06 seconds as indicated in the table: 2. The F_2 formulation containing 5% novel superdisintegrant i.e. modified starch disintegrated rapidly.

The results *in-vitro* wetting time and water absorption ratio were found to be within prescribed limits and satisfy the criteria of fast dissolving tablets (Fig.5). The in-*vitro* wetting time was decreased when the superdisintegrant was used. In the case of formulation F2 modified starch, the wetting item found to be 22±0.12sec, indicating the suitability of modified starch as novel superdisintegrant.

To evaluate the individual and combined effects of the factors involved, fast dissolving tablets were formulated employing selected combination of the factors as per 2^3-factorial design. The disintegration wetting time and release parameters (percent drug dissolved in 10 min and dissolution efficiency in 5 min) of the fast dissolving tablets formulated were analyzed as per ANOVA of 2^3- factorial design indicated that the individual, effects of modified starch (A), croscarmellose sodium (B), and crospovidone (C) as well as the combined effect of AB, AC, BC and (ABC) factors was significant on all the parameters analyzed. With in 53±0.5 seconds indicating the suitability of modified starch as superdisintegrants.

TABLE-5 ANOVA of Disintegration Time of Piroxicam Fast Dissolving Tablets

Source of variation	d. f	S.S	M.S.S	Variance ratio	Result
Replicates	2	2704.75	1352.37	22.80	$P < 0.05$
Treatments	7	21395501	3056500.14	5153.31	$P < 0.05$
Modified Starch(A)	1	761484.37	761484.37	12839.05	$P < 0.05$
Croscarmellose sodium (B)	1	65626.04	65626.04	1106.49	$P < 0.05$
Modified starch x Croscarmellose (AB)	1	474609.37	474609.37	8002.18	$P < 0.05$
Crospovidone (C)	1	408465.04	408465.04	6886.95	$P < 0.05$
Modified starch x Crospovidone (AC)	1	832165.04	832165.04	14030.77	$P < 0.05$
Croscarmellose x Crospovidone (BC)	1	65626.04	65626.04	1106.49	$P < 0.05$
Modified starch x Croscarmellose x Crospovidone (ABC)	1	474609.37	474609.37	8002.18	$P < 0.05$
Error	14	830.46	59.31	---	---
Total	23	8.27	0.35	---	---

*SD Standard Deviation from mean, n=3, P<0.05 indicate significance; P>0.05 indicate non-significance, d. f–Degree of Freedom
*S. S–Sum of Square *M. S. S–Mean Sum of Squares, ANOVA= Analysis of Variance

TABLE-6 ANOVA of Water Absorption Ratio of Piroxicam Fast Dissolving Tablets

Source of variation	d. f	S.Ss	M.S.S	Variance ratio	Result
Replicates	2	39.58	19.791	3.564	P < 0.05
Treatments	7	180847.62	25835.37	4652.50	P < 0.05
Modified Starch(A)	1	69660.37	69660.37	12544.62	P < 0.05
Croscarmellose sodium (B)	1	8400.04	8400.04	1512.70	P < 0.05
Modified starch x Croscarmellose sodium x(AB)	1	36738.37	36738.37	6615.94	P < 0.05
Crospovidone (C)	1	42588.37	42588.37	7669.43	P < 0.05
Modified starch x Crospovidone (AC)	1	13490.04	13490.04	2429.32	P < 0.05
Croscarmellose sodium x Crospovidone (BC)	1	6633.37	6633.37	1194.55	P < 0.05
Modified starch x Croscarmellose sodium x Crospovidone (ABC)	1	3337.04	3337.04	600.94	P < 0.05
Error	14	77.75	5.553	---	---
Total	23	180964.95	7868.04	---	---

*SD Standard Deviation from mean, n=3, P<0.05 indicate significance; P>0.05 indicate non-significance, d. f–Degree of Freedom
*S. S–Sum of Square *M. S. S–Mean Sum of Squares, ANOVA= Analysis of Variance

TABLE-7 ANOVA of Percent Drug Dissolved In 5 Minutes of Piroxicam Fast Dissolving Tablets

*SD Standard Deviation from mean, n=3, P<0.05 indicate significance; P>0.05 indicate non-significance, d. f–Degree of Freedom

Source of variation	d. f	S.S	M.S.S	Variance ratio	Result
Replicates	2	595955	29797.5	156.78	P < 0.05
Treatments	7	111309.33	1590.33	83.52	P < 0.05
Modified Starch(A)	1	3607.87	3607.87	18.94	P < 0.05
Croscarmellose sodium (B)	1	1374.4093	1374.4093	7.2	P < 0.05
Modified starch x Croscarmellose sodium x (AB)	1	2171.703	2171.703	11.40	P < 0.05
Crospovidone (C)	1	890.3580	890.3580	4.67	P < 0.05
Modified starch x Crospovidone(AC)	1	2041.67	2041.67	10.72	P < 0.05
Croscarmellose sodium x Crospovidone (BC)	1	1052.05	1052.05	5.5	P < 0.05
Modified starch x Croscarmellose sodium x Crospovidone (ABC)	1	1597.07	1597.07	8.3	P < 0.05
Error	14	2665.76	190.41	---	---
Total	23	12672.54	550.9802	---	---

*S. S–Sum of Square *M. S. S–Mean Sum of Squares, ANOVA= Analysis of Variance

TABLE-8 ANOVA of Dissolution Efficiency in 5 Min of Piroxicam Fast Dissolving Tablets

Source of variation	d.f	S.S	M.S.S	Variance ratio	Result
Replicates	2	111.26	55.98	7.23	$P < 0.05$
Treatments	7	12902.45	1843.23	255.97	$P < 0.05$
Modified Starch(A)	1	4425.45	4425.45	571.76	$P < 0.05$
Croscarmellose sodium (B)	1	1139.88	1139.88	147.27	$P < 0.05$
Modified starch x Croscarmellose sodium (AB)	1	1780.20	1780.20	230	$P < 0.05$
Crospovidone (C)	1	1058.68	1058.68	136.78	$P < 0.05$
Modified starch x Crospovidone (AC)	1	670.98	670.98	86.69	$P < 0.05$
Croscarmellose sodium x Crospovidone (BC)	1	1014	1014	131.68	$P < 0.05$
Modified starch x Croscarmellose sodium x Crospovidone (ABC)	1	3717.57	3717.57	480.30	$P < 0.05$
Error	14	108.49	7.74	---	---
Total	23	544053.77	23654.51	---	---

*SD Standard Deviation from mean, n=3, P<0.05 indicate significance; P>0.05 indicate non-significance, d. f–Degree of Freedom
*S. S–Sum of Square *M. S. S–Mean Sum of Squares, ANOVA= Analysis of Variance

ANOVA of disintegration time, wetting time, percent drug dissolved and dissolution efficiency in 5 min (Table: 7.5, 7.6, 7.7, 7.8) indicated that the individual effect as well as combined effects of the three factors (i.e., modified starch, croscarmellose sodium and crospovidon) were all significant ($p<0.05$). The ANOVA results, thus indicated that the three factors have significantly influence the disintegration time, wetting time, percent dissolved in 10 min and dissolution efficiency in 5min.

Piroxicam fast dissolving tablets (F_2) formulated employing modified starch (5%), as novel superdisintegrant exhibited good disintegration and dissolution efficiency in 5 min. Formulation F_2 gave release of 99.89±12%in 10 min fulfilling the official specification, based on disintegration on time and dissolution efficiency in 5 min,. F2 is considered as a good fast dissolving tablet formulation of piroxicam.

A polynomial regression algorithm was used to relate the independent variables to the response variables. The general second order model equation that could be constructed from 2^n experimental design is in indicated in equation (1).

$Y= \beta_0 + \beta_1 A + \beta_2 B + \beta_3 C + \beta_1\beta_2 AB + \beta_1 \beta_3 AC + \beta_2\beta_3 BC + \beta_1\beta_2 \beta_3 ABC$ ---- Eq(1).

Where Y is the measured response, β_0 is the arithmetic mean response of 8 runs , $\beta_1, \beta_2, \beta_3, \beta_1\beta_2, \beta_1 \beta_3, \beta_2\beta_3, \beta_1\beta_2 \beta_3$ are the coefficients for the corresponding factors, and A, B, C, AB, AC, BC and ABC are the percentages of modified starch (A) , croscarmellose sodium (B) and crospovidone (C) and interaction terms respectively. The co-efficients were calculated according to the general formula given in equation 2^7.

$\beta = \Sigma XY/2^n$ ----Eq (2)

where β is the coefficient, X is the corresponding variable (A,B,C) and Y is the response value (dissolution efficiency in 5 minutes) and n is the level.

The two levels of the three factors employed in the experimental design are indicated in Table 9 and transformed design for analysis of responses of piroxicam fast dissolving tablets is shown in Table 10.

Table 9: Levels of the three factors used in the experimental design

Factors		Levels	
Ingredient	**Code**	**L_1**	**L_2**
Modified Starch	A	0	5
Croscarmellose sodium	B	0	5
Crospovidone	C	0	5

Table 10: Transformed design for analysis of responses of Piroxicam Fast Dissolving Tablets

Formula code	A(%)	B(%)	C(%)
F1	0	0	0
7F2	5	0	0
F3	0	5	0
F4	5	5	0
F5	0	0	5
F6	5	0	5
F7	0	0	5
F8	5	5	5

The dissolution efficiency in 5 minutes, dissolution data clearly indicate that the dependent variables are strongly dependent on the independent variables. The fitted equations relating the response dissolution efficiency in 5 minutes to the transformed factor is shown in equations 3.

Final Equation in Terms of Coded Factors:

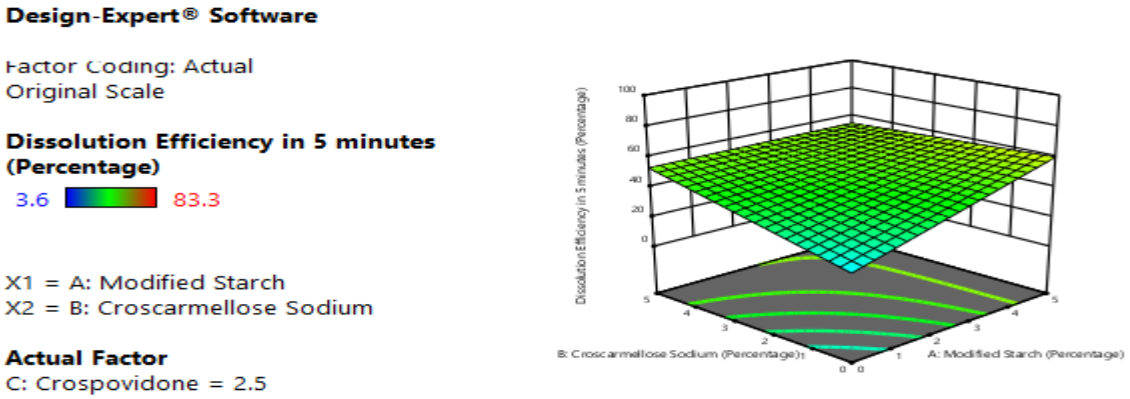
Dissolution efficiency in 5 minutes =
+47.69+9.81A+6.24B+5.81C-8.89AB-8.56AC+
7.81BC+12.59ABC(R^2 = 1.000) ---Eq (3)

The value of the R^2 indicates a good fit. The polynomial equations can be used to draw a conclusion after considering the magnitude of coefficient and the mathematical sign it carries (positive or negative).

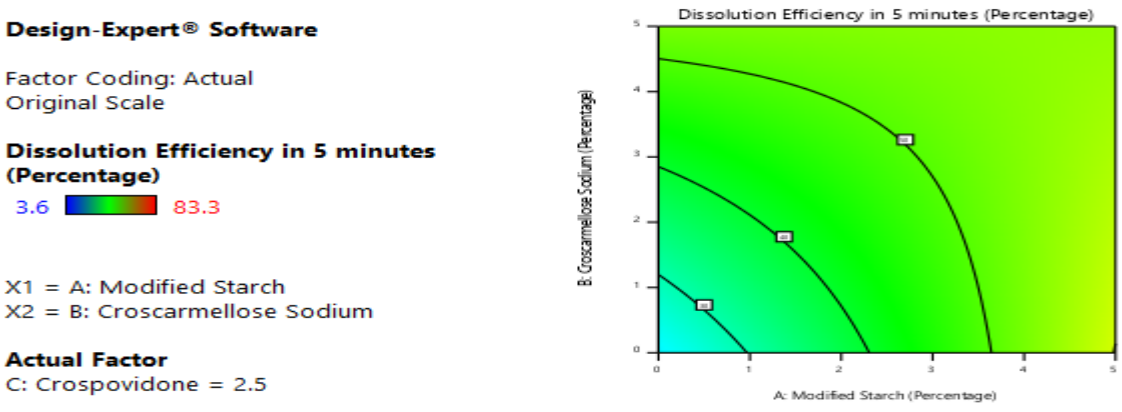
From the polynomial equations, one can easily deduce that the effect of interactions between modified starch and croscarmellose sodium (AB); modified starch and crospovidone (AC); croscarmellose sodium and crospovidone (BC) are significant on the dissolution efficiency in 5 minutes but negatively in case of interaction between A&B, and A&C, but positively in case of interaction between B&C. On contrary, the magnitudes of coefficients of modified starch (A), croscarmellose sodium (B), crospovidone (C) and interaction between modified starch, croscarmellose sodium and crospovidone (ABC) are larger and positive, showing that the dissolution efficiency in 5 minutes of piroxicam fast dissolving tablets is affected by all A, B, C and ABC in positive manner. The equation for dissolution efficiency in 5 minutes suggests that the factor A has more significant effect on dissolution efficiency in 5 minutes followed by factor B, C.

Once, the polynomial equation which relates the levels of each factor and their corresponding interactions with dissolution efficiency in 5 minutes was derived, the surface response curves and contour plots were constructed using Stat Ease, Inc. (Minneapolis, MN) Design Expert 11 Version software.

Fig.6: (A) Response Surface Plot (B) Contour Plot of Piroxicam Fast dissolving tablets. (effect of Modified starch and Croscarmellose sodium on Dissolution efficiency in 5 minutes).

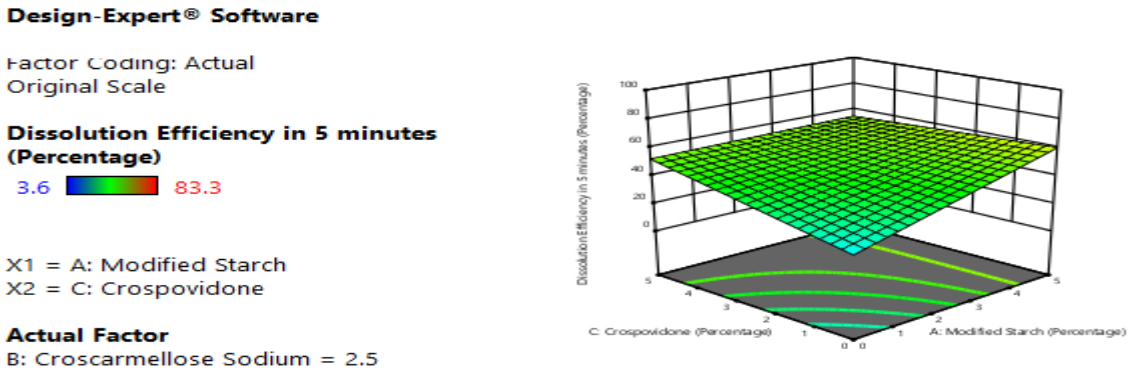


(A) Response Surface Plot

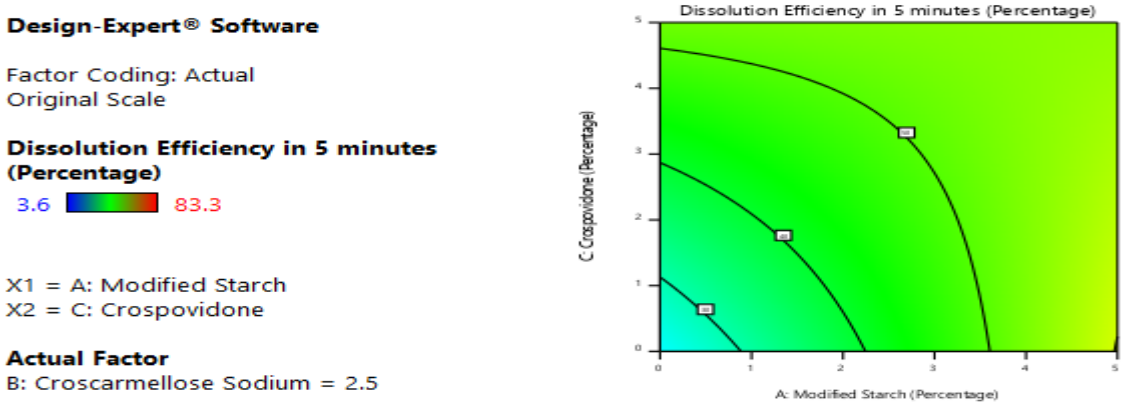


(B) Contour Plot

Fig.7: (A) Response Surface Plot (B) Contour Plot of Piroxicam Fast dissolving tablets. (effect of Modified starch and Crospovidone on Dissolution efficiency in 5 minutes).

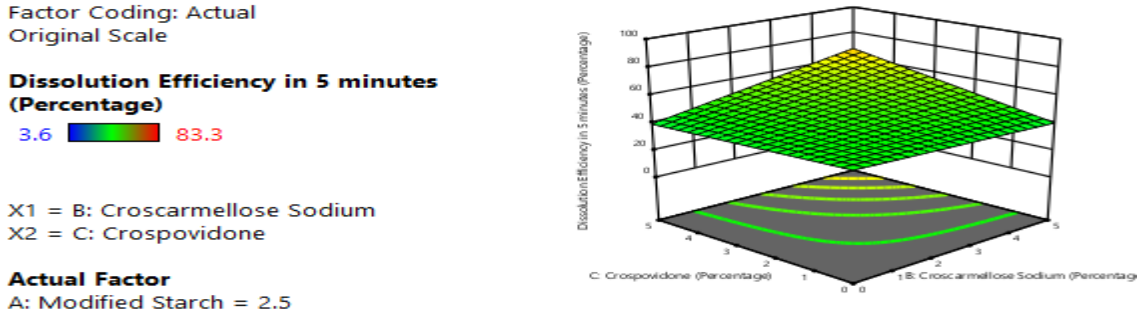


(A) Response Surface Plot

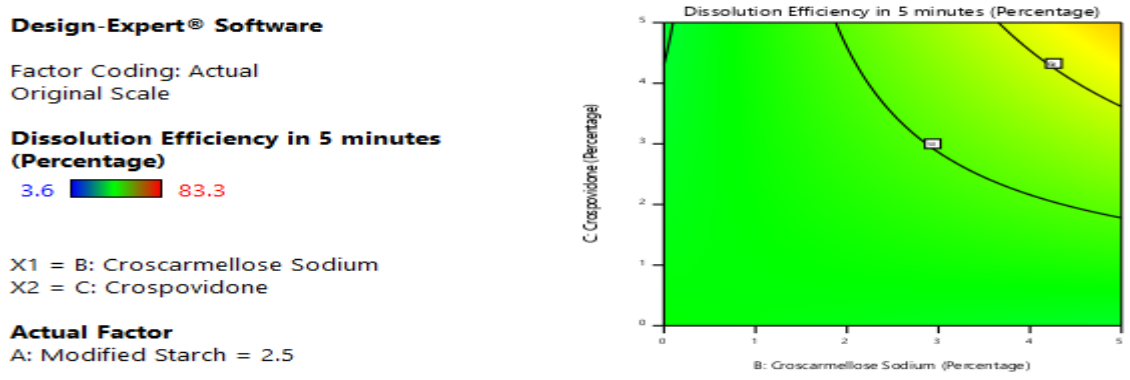


(B) Contour Plot

Fig.8: (A) Response Surface Plot (B) Contour Plot of Piroxicam Fast dissolving tablets. (effect of Crospovidone and Croscarmellose sodium on Dissolution efficiency in 5 minutes)



(A) Response Surface Plot



(B) Contour Plot

The response surface plots and contour plots reveal that as the concentration of modified starch (A) increases, dissolution efficiency in 5 minutes increases. The other two variables also croscarmellose sodium (B) and crospovidone (C) have a positive effect on dissolution efficiency in 5 minutes i.e., as the concentrations of B and C increases, dissolution efficiency in 5 minutes also increases. The effects of A and B on dissolution efficiency in 5 minutes are shown in Fig 6. The contour plots were found to be almost linear indicating a linear relationship between A and B on dissolution efficiency in 5 minutes. It was determined from the contour plot (Fig 6 B), that a higher dissolution efficiency in 5 minutes can be obtained with an A level range between 4 to 5 %, and a B level range from 4-5 %. It is evident from contour plot that the high levels of A and high levels of B favors dissolution efficiency in 5 minutes of piroxicam fast dissolving tablets. The effects of A and C on dissolution efficiency in 5 minutes are shown in Fig 7. The contour plots were found to be linear indicating a linear relationship between A and C on dissolution efficiency in 5 minutes. It was determined from the contour plot (Fig. 7 B), that a higher dissolution efficiency in 5 minutes can be obtained with an A level range between 4 to 5 %, and a C level range from 4 – 5 %. It is evident from contour plot that the low levels of A and high levels of C favors dissolution efficiency in 5 minutes of piroxicam fast dissolving tablets. The effects of B and C on dissolution efficiency in 5 minutes are shown in Fig 8. The contour plots were found to be linear indicating a linear relationship between B and C on dissolution efficiency in 5 minutes. It was determined from the contour plot (Fig. 8 B) that higher dissolution efficiency in 5 minutes can be obtained with a B level range between 4 to 5 %, and a C level range from 4-5 %. It is evident from contour plot that the high levels of B and C favors dissolution efficiency in 5 minutes of piroxicam fast dissolving tablets.

Comparison of Optimized Piroxicam acid Fast Dissolving Tablet (F2) with the Marketed Sample (Mobicam) :

The optimized formula was compared with the marketed formula (Mobicam). The physical properties of optimized piroxicam fast dissolving tablets (F2) and the marketed formulation (MOBICAM) were almost similar.

Table 11: Physical properties: Hardness, Friability, Drug Content, Wetting Time, Water Absorption Ratio of Optimized Piroxicam Fast Dissolving Tablet (F2) employing modifies starch and Marketed Formulation (Mobicam).

Formul-ation code	Hardness (Kg/Cm²) ±S.D	Friability (%)±S.D	Drug Content±S.D	Disintegration Time (S)±S.D	Wetting Time (sec)±S.D	Water Absorption Ratio(%)±S.D
Mobicam	3.9±0.02	0.1±0.012	17.26±0.13	25±0.1	20±0.2	1.57±0.1
F2	3.7±0.03	0.13±0.015	19.21±0.2	53±0.5	22±0.12	1.89±0.18

*SD standard deviation from mean, n=3, mean±SD.

Table: 12. Dissolution Data of Optimized Piroxicam Fast Dissolving Tablets Employing Modified starch (F2) and Marketed Formulation

Piroxicam Percent Dissolved from Fast Dissolving Tablets		
Time (Min)	Mobicam	F2
5	84.18±0.11	85.12±0.2
10	97.81±0.21	99.89±0.4

*SD standard deviation from mean, n=3, mean±SD.

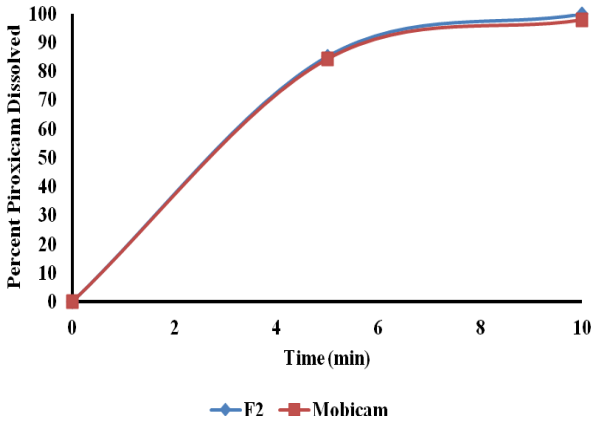


Fig. 9: Dissolution Profiles of Optimized Piroxicam Fast Dissolving Tablets Employing Modified starch and Marketed Formulation. (F & Mobicam)

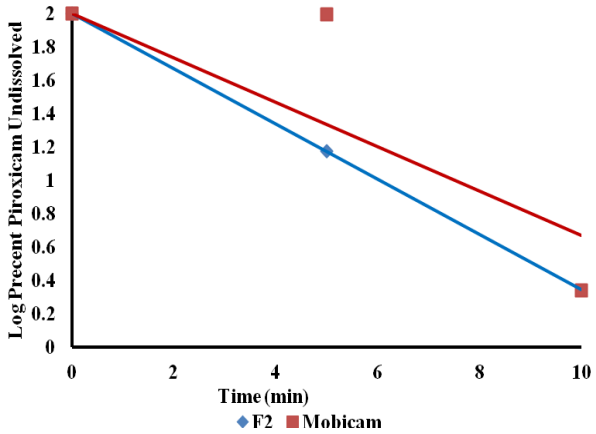


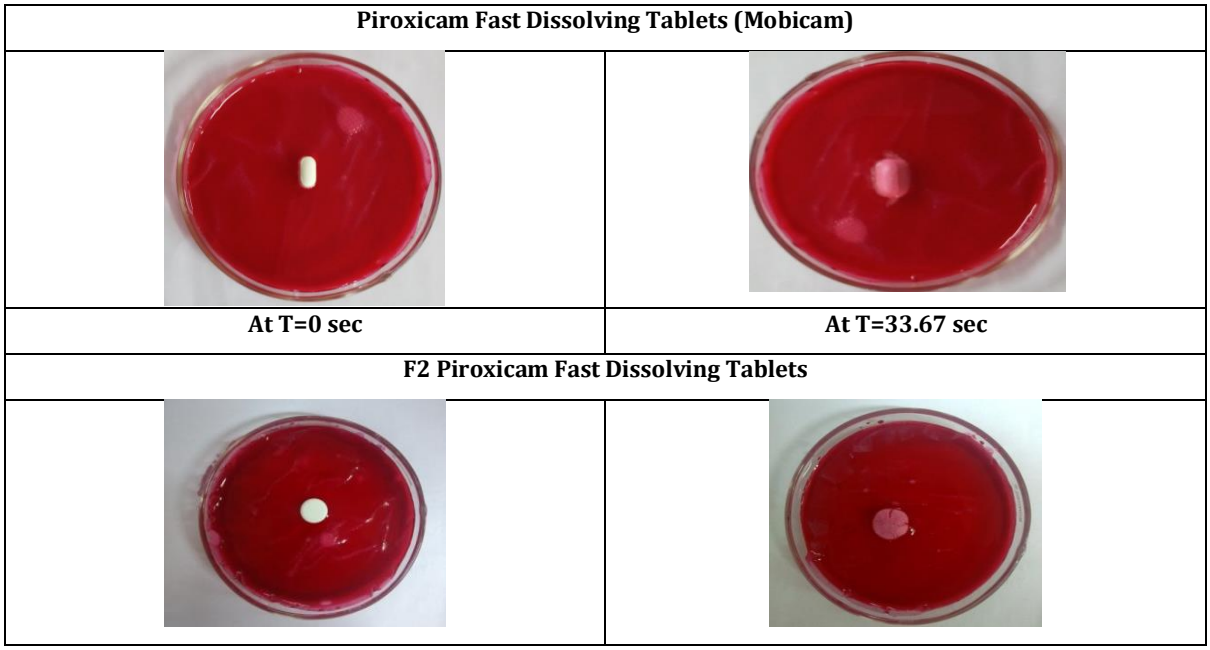
Fig 10: Log Time Vs Log Percent Undissolved of optimized Piroxicam Fast Dissolving Tablets Employing Modified starch and marketed formulation (F2 & Mobicam)

Table 13: Dissolution Parameters of Optimized Piroxicam Fast Dissolving Tablets Formulated Employing Modified starch (F2) and Marketed Formulation (Mobicam)

Parameters	Mobicam	F2
PD_5	84.18±0.13	85.12 ± 0.74
DE_5 (%)	80.5	83.3
K_1 (min^{-1})	0.3316	0.3915

*SD standard deviation from mean, n=3, mean±SD, PD_5-Percent dissolved in 5 min., DE_5%-Dissolution efficiency in 5 min., K_1 =First order rate constant

Fig: 9 Wetting Times of Optimized Piroxicam Fast Dissolving Tablets Employing Modified starch and marketed formulation (F2 & Mobicam)



CONCLUSION:

Modified starch is an efficient superdisintegrant for fast dissolving tablets. Drug release from the prepared tablets was rapid and is with in 10min and depended on the composition of the tablet i.e., concentration of modified starch, croscarmellose sodium and crospovidone. Based on the results obtained from polynomial equations and response surface methodology, the individual effects of modified starch (A), croscarmellose sodium (B) and crospovidone (C) and interaction between ABC are more significant and positive effect on dissolution efficiency in 5 Response surface plots and contour plots indicated that the dissolution efficiency in 5 minutes of piroxicam fast dissolving tablets is influenced mostly by modified satrch, followed by croscarmellose sodium and crospovidone. Fast dissolving tablets (F2) formulated employing modified starch (5%), croscarmellose sodium (0%) and crospovidone (0%) exhibited rapid disintegration and fast release of drug with in 10 minutes.

Optimization of piroxicam fast dissolving tablets is a complex process when a new starch based superdisintegrnt, modified starch is used as a superdisintegrant, which requires to consider a large number of variables and their interactions with each other. The present study conclusively demonstrates the use of 2^3– factorial design in optimization of piroxicam fast dissolving tablets. The derived polynomial equations and contour plots aid in predicting the values of selected independent variables for preparation of piroxicam fast dissolving tablets with desired properties.

The optimized formulation (F2) gives the best result in terms of the required disintegration time, dissolution efficiency in 5 minutes, and drug release was in accordance with the USP dissolution criteria for conventional tablet of piroxicam drug. It is thus concluded that by adopting systematic approach, an optimum point can be reached in shortest time with minimum efforts when modified starch, is used as a superdisintegrant for achieving fast dissolving formulations.

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