Research Article

Determination of Release Kinetics of Oxaprozin (*A Model Drug*) From Oral Fast Dissolving Films Prepared Using HPMC and CMC

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ABSTRACT
Aim of present research investigation is to formulate and evaluate in –vitro parameters of oral fast dissolving films, Oxaprozin a non steroidal anti-inflammatory drug acts as a model drug in this present investigation in an approach to increase bioavailability of the drugs formulated in oral films rather than other type of oral dosage forms. Oral fast dissolving films of Oxaprozin were prepared using Hydroxy Propyl Methyl Cellulose, Ac-di-sol, Carboxy Methyl Cellulose and Sodium Starch Glycolate. OFDs films were prepare by using a fast and versatile solvent-casting method. OFDs films were evaluated for film characteristics and in-vitro parameters. Weights of the films are in between 197 mg to 206 mg, thickness was found to be 0.16 mm to 0.29 mm, where as folding endurance of the prepared film found to be 98 to 108 times, in surface pH study all films were found to be neutral, with content uniformity in films was from 95.2 to 98.4 percent, and disintegration time rage form 3 min. to 6 min. and drug release was 97.7% in 15 minutes for formulation F-5. Release kinetics studies were determined for F-5 in zero order, first order, Higuch plot and koymer Peppas model, of which the sequence of regression R^2 was found to be as HIGUCHI >>>ZERO ORDER>>FIRST ORDER>KOYMER PAPPAS. The R^2 was found to be 0.9994. Formulation F-5 was optimized and taken for one month stability studies, where all invitro evaluation parameters were meeting standard specifications.

Key words: Oxaprozin, HPMC, Ac-di-sol, CMC; SSG.

1. INTRODUCTION

Oral drug delivery system is an ancient commonly administered route of pharmaceutical dosage forms for its advantages of easy administration, handling[1]. The step for formulation of fast dissolving drug delivery systems were started in early 1970's, the major advantage of fast dissolving films are to bypass hepatic first pass drug metabolism and to increase bioavailability[2]. Oxaprozin an anti-inflammatory agent used as a model drug to study the all physical characteristics and release kinetics[3]. In the present study Oxaprozin fast dissolving films were prepared by using Hydroxy Propyl Methyl Cellulose, Sodium Carboxy Methyl Cellulose and Cross Carmellose Sodium[4].

2. MATERIALS AND METHODS

2.1 MATERIALS

Oxaprozin was acquired from Gold fish Pharma limited, HYDERABAD.
HPMC, NaCMC, Croscarmellose sodium and other excipients used in present work was purchased from SD fine chemicals, HYDERABAD.

2.2 Preparation of Oxaprozin oral fast dissolving films by Solvent Casting Method[5]:

Oral fast dissolving films of Oxaprozin 0077ere prepared first by dissolving strip and film forming agents Hydroxy Propyl Methyl Cellulose, Carboxy Methyl Cellulose in distill water, then the solutions were continuously stirred up to four hours on magnetic stirrer and kept for 2 hours to remove air.

Mean while in the separate container remaining water soluble substances like sweetening agents, flavor agents and drug were dissolved in water with constant stirring for 45 minutes. In the next step both the solutions was mixed with constant stirring for one hour on magnetic stirrer. After mixing the solution was kept for aside for settling foam produced during mixing. The final prepared solution was casted on a plate, which was dried for 24 hours at room temperature. The dried films were removed and cut in to uniform dimensions strips, wrapped in butter paper covered with aluminum foil and were stored in desiccators. The details of formulations are given below table no. 01.

Table 1: Formulation of Oxaprozin films

s.no	Ingredient	F-1	F-2	F-3	F-4	F-5	F-6	F-7
1	Oxaprozin	30	30	30	30	30	30	30
2	SSG	0.2	0.4	-	0.8	-	1%	-
3	CCS	-	-	0.5%	-	1%	-	1.5%
4	HPMC	2%	3%	4%	5%	3%	-	-
5	CMC	-	-	-	-	-	4%	4%
6	PEG-400	0.1%	0.1	0.1%	0.1	0.1	0.1%	0.1%
7	Inference	No	Yes	Yes	Yes	Yes	Yes	Yes

2.3 Evaluation of oral fast dissolving films

2.3.1 Weight variation test[6]

3*4 cm^2 films are made in prepared films and weight of each strip was determined and weight variation was calculated was calculated.

2.3.2 Thickness of the film[7]

Measuring thickness of films was determined by digital Vernier calliper at three places of films and standard deviation was calculated with a least count of 0.01 mm at different spots of the film.

2.3.3 Folding endurance[7]

It is measurement of flexibility of the films which resist brittleness, where film starts breaking in number of folds done. A piece of 3*4 cm film made to subject for performance the test till it breaks and number folding were noted.

2.3.4 pH studies[8]

The pH was determined by dissolving a film in 2 ml of distilled water and then the pH of the obtained solution was measured by pH paper.

2.3.5 Drug Content uniformity[9]

Oxaprozin was analyzed using UV SPECTROSCOPY from all formulations For this, each strip at three different places equivalent to 35mg of drug was cut and dissolved in 50ml of 6.8Ph phosphate buffer solution with continuous stirring. This solution was filtered using Whattmann filter paper, and the filtrate was diluted to 100ml with the same buffer in a volumetric flask. This solution was analyzed by U.V.Spectrophotometer and the absorbance was recorded at 250nm. Drug content was calculated by using calibration curve of drug.

2.3.3 Disintegration time[9]

Test was performed using disintegration test apparatus. 2×3 cm^2 film was placed in the basket, raised and lowered it in such a manner that the complete up and down movement at a rate equivalent to ten times a minute. Time required by the film, when no traces of film remain above the gauze was noted. Test was performed in triplicate.

2.3.4 Invitro Dissolution studies[10]

Dissolution study was carried out using USP type I (basket apparatus) with 300 ml of 6.8 pH Phosphate buffer as dissolution medium maintained at 37 $\pm 0.5^0$ C. Medium was stirred at 50 rpm for a period of 30 minutes. Samples were withdrawn at every 1 min interval up to 30 min, replacing the same amount with the fresh medium. Samples were suitable diluted with 6.8 pH and analyzed for drug content at 250 nm. Cumulative percent drug release of Oxaprozin was calculated and plotted against time. The results are given in the table.

2.3.5 Data Analysis[10,11]

To analyze the mechanism of the drug release kinetics of the dosage form, the data obtained were fitted to various kinetic equations of zero order, first order, Higuchi model and Korsmeyer - Peppas model and plotted as:

1. Cumulative percent drug released Vs time(Zero order plots)
2. Log cumulative percent drug remaining Vs time(First order plots)
3. Cumulative percent drug release Vs square root of time(Higuchi plots)
4. log cumulative percent drug release Vs log time(Korsmeyer-Peppas Plots)

2.3.9 Zero Order Kinetics

Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the equation:

$$Q_0 - Q_t = K_0 t$$

Where, Q_t is the amount of drug dissolved in time t,
Q_0 is the initial amount of drug in the solution(most times,Q_0=0)
K_0 is the zero order release constant expressed in units of concentration/time.
When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys zero-order release kinetics, with slope equal to K_0.

2.3.10 First order kinetics

The release of the drug which followed first order kinetics can be expressed by the equation:

$$\text{Log } C = \log C_0 - K_t / 2.303$$

Where, C_0 is the initial concentration of drug,
k is the first order rate constant
t is the time.
The data obtained are plotted as log cumulative percentage of drug remaining vs. time which would yield a straight line with a slope of -K/2.303.

2.3.11 Higuchi model

The release of the drug which follows Higuch kinetics can be expressed by the equation:

$$Q = K_H * t_{1/2}$$

Where, K_H is the Higuchi dissolution constant
Q is the amount of drug released in time t
The data obtained were plotted as cumulative percentage drug release versus square root of time.

2.3.12 Korsmeyer-Peppas model

To find out the mechanism of drug release, drug release data were fitted in Korsmeyer-Peppas equation which is expressed as:

$$Q/Q_0 = k\, t^n$$

Q/Q_0 was fraction of drug released at time t,
K was constant and n was diffusion constant that indicates general operating release mechanism for Fickian (diffusion controlled) n ≤0.5; for non Fickian (anomalous/zero order) release '**n**' value is in between 0.5 to 1.0; for zero order release n=1.0; for super case transport II, n >1.0.
To study the release kinetics, data obtained from in vitro drug release studies were plotted as log cumulative percentage drug release versus log time.

3RESULTS AND DISCUSSIONS

3.1 Evaluation of Fast Dissolving Oral Films

3.1.1 Weight uniformity test

The weights of the films were found to be in the range of 197mg to 206mg. The results of average weight of all films were summarized in table no.02 and diagrammatically given in figure 02.

3.1.2 Physical appearance and surface texture

The observation by visual inspection of films and by feel or touch, suggests that the films are having smooth surface and they are elegant enough to see.

3.1.3 Thickness of films

The thicknesses of the films were in the range of to 0.16mm to 0.29mm. The results of average thickness of all films were summarized in table no.02 with graphical representation in figure no. 03

3.1.4 Folding endurance

Folding endurance of the films was found to be in the range of 98 to108.The results of average folding endurance of all films were summarized in table no.02.

3.1.5 Surface pH

The surface pH of all the films were found to be neutral as there was no color change in the litmus paper.

3.1.6 Drug content uniformity test

The drug content uniformity is performed by taking three films in each formulation trial and the average drug content was calculated. The results were found to be in the range of 94.4% to 98.9%. The results of average drug content of all films were summarized in table no.02 with graphical representation in figure 04.

3.1.7 Invitro disintegration test

The disintegration times of the prepared films were in the range of 3 min to 6 mins. The results of average disintegration time of all films were summarized in table no 03.

Table 2: Evaluation parameters of Oxaprozin

Code	Weight in mg	Thickness in mm	Folding endurance	Drug content %
F2	206	0.22	103	97.2
F3	203	0.29	108	95.8
F4	201	0.18	106	95.6
F5	198	0.17	98	98.9
F7	197	0.16	101	96.8
F8	205	0.21	104	94.4
F9	206	0.22	101	96

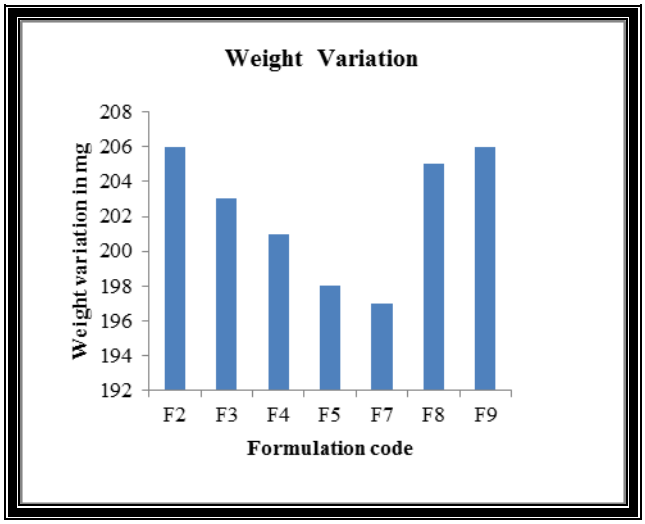

Fig. 1: weights of the films from F2-F5and F7-F9

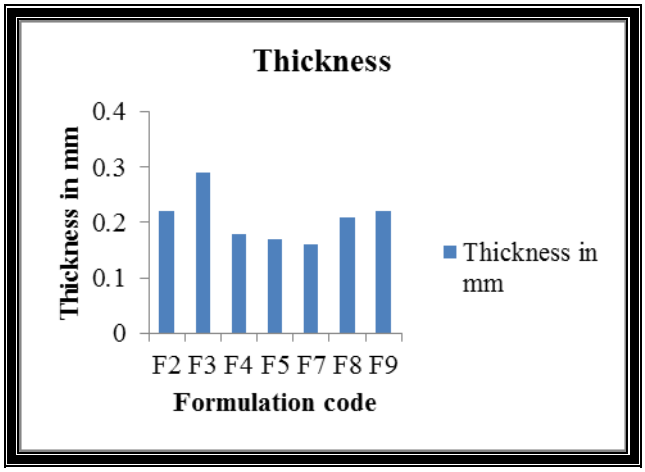

Fig. 2: Thickness of the films from F2-F5and F7-F9

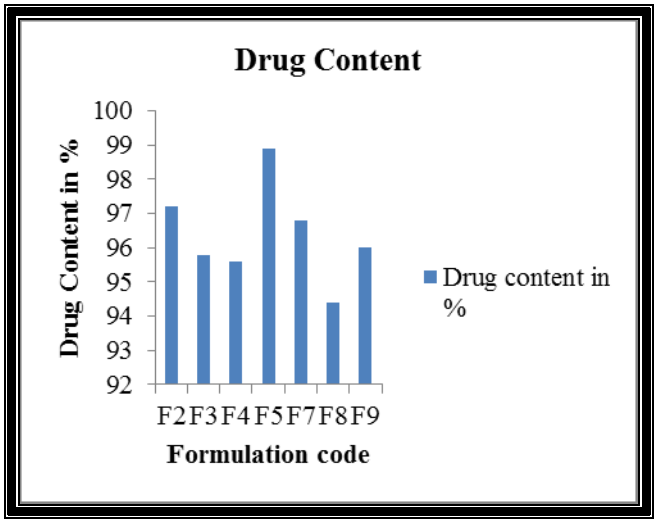

Fig. 3: Drug content of the films from F2-F5and F7-F9

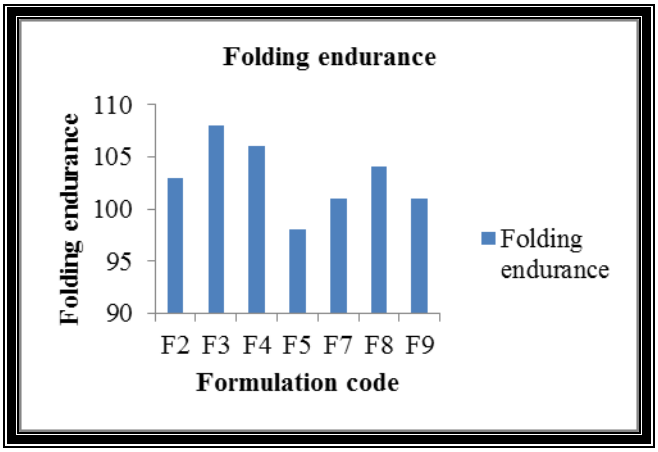

Fig. 4: Folding endurance of the films from F2-F5and F7-F9

3.1.8 Invitro dissolution studies

Oxaprozin FDOF dissolution study was conducted in 6.8pH phosphate buffer solution as this was similar to the pH of simulated salivary fluid. A modified dissolution methodology was followed to simulate the conditions of the oral cavity. The dissolution volume consists of 300ml of 6.8pH phosphate buffer solution at 37±0.5˚C, which was rotated at 50rpm. Oxaprozin FDOF from each formulation was carried out in 6.8 pH phosphate buffer solution for 20min. The data of dissolution studies were summarized in table no. 03. The dissolution study was conducted for 15 min. The drug release was found to be in the range of 65.8% to 98.7% and the % drug release was maximum. The

plots of % cumulative drug release versus time (min) were plotted and depicted as shown in Fig.05. The formulation F5 showed higher drug release of 98.7% revealing that films made with concentrations of HPMC., 3%w/v and CCS 1% w/v was the optimized formulation as it shows a higher drug release in the dissolution study. As higher dissolution rate aids in faster onset of action, F5 was chosen as the optimized formulation.

Table no. 03: Invitro drug release data of formulation F2-F5 and F7 to F9

Time	F2	F3	F4	F5	F7	F8	F9
2	15.8	11.6	19.3	35.6	13.3	9.5	20.8
4	30.8	27.7	34.7	48.3	28.8	24.6	36.2
6	42.6	39.1	46.8	60.8	41.7	37.6	47.3
8	50.8	46.2	55.3	69.6	48.6	44.8	56.6
10	59.1	57.2	64.8	79.3	58.5	54.7	65.9
15	70.6	68.3	75.3	97.7	69.2	64.8	76.8

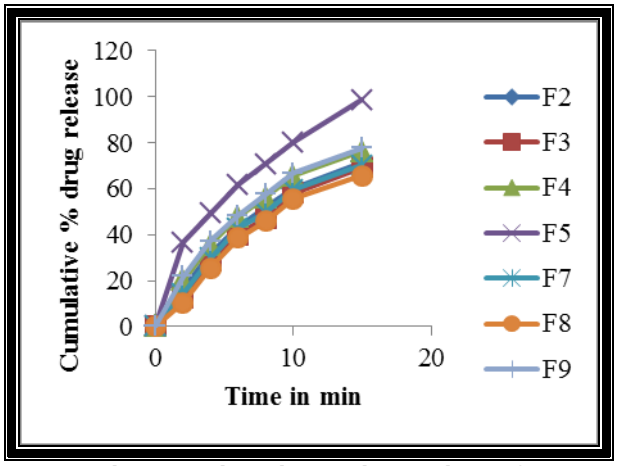

Fig. 5: Invitro drug release data of formulations F2-F5 and F7-F9

3.1.9 **Data analysis (Curve fitting analysis)**

For analyzing the mechanism of the drug release kinetics of the dosage form, the data obtained were fitted to various kinetic equations of Zero order, First order, Higuchi model and Korsmeyer - Peppas model. The regression coefficient is calculated. The data of regression coefficient of different kinetic models were summarized in table no.04.

Table 4: Oxaprozin release kinetics data from (F5 optimized formulations)

	ZERO	FIRST	HIGUCHI	PEPPAS
	% CDR Vs T	Log % Remain Vs T	%CDR Vs √T	Log C Vs Log T
Slope	6.00733	-0.11398	25.34912	1.43333
Intercept	18.13853	2.156477	-0.19652	0.5674
R	0.950970	-0.93512	0.999691	0.85104
R 2	0.904345	0.874457	0.99938	0.72428

Regression data of Oxaprozin from F5 (Optimized Formulation) Graphical representation

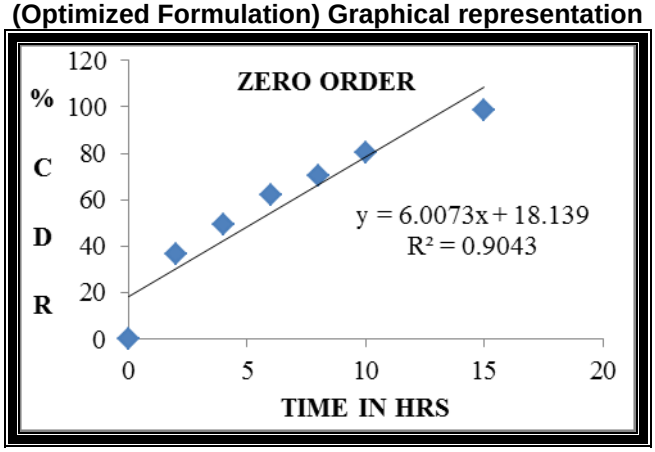

Fig. 6: zero order kinetics

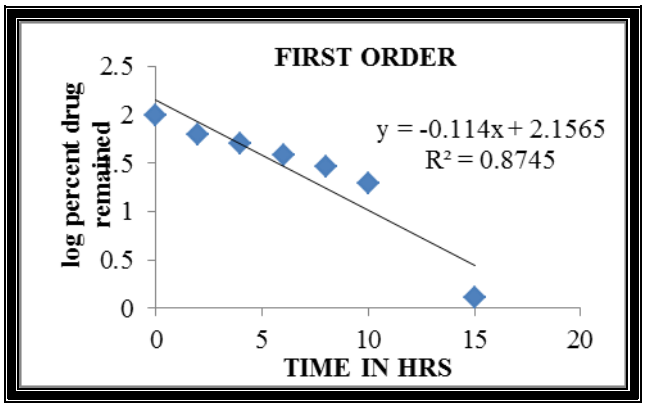

Fig. 7: First order kinetics

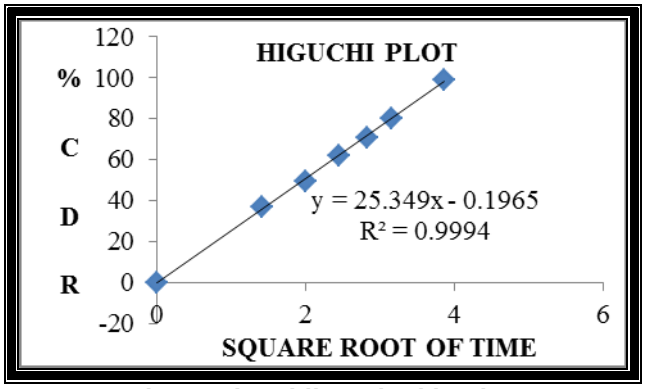

Fig. 8: Higuchi's order kinetics

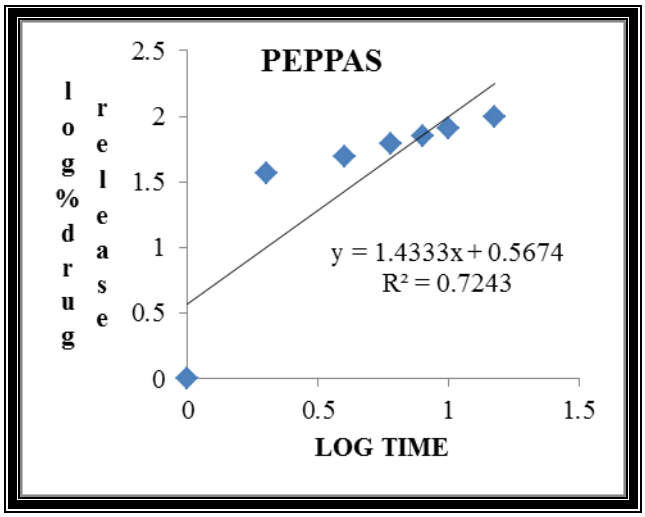

Fig. 9: Peppa's order kinetics

4 CONCLUSION

Present study reveals that all the seven formulated films showed satisfactory film parameters. It can be concluded that, Oral fast dissolving film-containing Oxaprozin can be prepared by solvent casting method. 3% w/v of HPMC and 1% CCS (F5) film exhibited required folding endurance and disintegration time. The drug release was about 98.7 % in 15min.

From the present investigation it can be concluded that oral fast dissolving film formulation can be a potential novel drug dosage form for pediatric, geriatric and also for general population.

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