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FORMULATION AND EVALUATION FAST DISSOLVING FILM OF LORNOXICAM

Shweta S. Patil*, Yuvraj J Mane, Shrinivas K Mohite, Chandrakant S. Magdum

Department of Quality Assurance, Rajarambapu College of Pharmacy, Kasegaon, Tal.Walwa, Dist Sangli 415404, M.S. India.

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For Correspondence:

Shweta S. Patil

Department of Quality Assurance, Rajarambapu College of Pharmacy, Kasegaon, Tal.Walwa, Dist Sangli 415404, M.S. India

E-mail:

patilshweta320@gmail.com

ABSTRACT

The aim of the present study is to formulate and evaluate the immediate release oral dispersible film formulation of Lornoxicam with different ratios of polymeric combinations by the solvent evaporation technique. Lornoxicam a potent Non Steroidal Anti-Inflammatory Drug (NSAID) with shorter half life makes the development of immediate release dosage forms extremely advantageous. These formulations are studied for physical appearance, thickness uniformity, weight uniformity, folding endurance, percent moisture absorption, determination of surface PH, drug content uniformity, swelling study, in vitro drug release study and dissolution study. The developed fast dissolving films increases the efficacy of Lornoxicam for the therapy of Arthritis and other painful muscular condition.

INTRODUCTION

Despite of tremendous advancement in drug delivery the oral route of drug administration is the most important method of administration of drug for systemic effect. Oral route is most preferred route by medical practitioners and manufacturer due to highest acceptability of patients. About 60% of all dosage forms available are the oral solid dosage form. The lower bioavailability, long onset time and dysphasia patients turned the manufacturer to the parentrals and liquid orals. But the liquid orals (syrup, suspension, emulsion etc) have the problem of accurate dosing mainly and parentrals are painful drug delivery, so most patient incompliance. Each pharmaceutical company wants to formulate the novel oral dosage form which has the higher bioavailability, quick action and most patient compliance.[1,3]

Difficulty in swallowing (dysphasia) is common among all age groups, especially in elderly, and is also seen in swallowing conventional tablets and capsules. An estimated 35% of the general population, and an additional 30-40% of elderly institutionalized patients and 18-22% of all persons in long-term care facilities, suffer from dysphasia. This disorder is associated with many medical conditions, including stroke, Parkinson's, AIDS, thyroidectomy , head and neck radiation therapy, and other neurological disorders, including cerebral palsy.

"A thin flexible, non-friable polymeric film having dispersed active pharmaceutical ingredient which is intended to be placed on the tongue for rapid disintegration and dissolution in the saliva prior to swallowing for delivery into GIT. Lornoxicam is a newer NSAID of oxicam class. It is a strong analgesic and anti- inflammatory agent. Its analgesic activity is comparable to that of opioids (more effective than 10 mg morphine when used at doses > or =8 mg to control pain after oral surgery). Clinical investigations have established it as a potent analgesic with excellent anti-inflammatory properties in a range of painful and/or inflammatory conditions including Rheumatoid arthritis and postoperative pain.[6]

MATERIALS AND METHODS

Materials

All the polymers of the formulation like HPMC and others are purchased from research lab, Islampur. Lornoxicam is obtained as a gift sample from Aristo Pharmaceuticals, Mumbai. All the other laboratory chemicals used in the study were of analytical reagents grade. Double distilled water was used throughout the study.

Method

1) Preformulation studies:- Preformulation studies were performed to determined the physicochemical properties of drug that could affect the development and efficiency of new drug formulations.

2) (i) Preparation of complex of Lornoxicam with β-cyclodextrin[7]

A mixture of lornoxicam and β-cyclodextrin was ground in a glass container and a minimum amount of water was added. The mixture was stirred for 5 min and dried at 60°C in the vacuum oven. After drying inclusion complex of lornoxicam and β-cyclodextrin was obtained.

(ii) Characterization of complex for drug content

Drug content was determined by dissolving 25 mg of complex in suitable quantity of 0.1N HCl and analyzed 1mL of appropriately diluted sample at 376 nm using UV-vis spectrophotometer, Shimadzu 1800

Table 1 : ***Drug content of prepared complex***

Serial No. complex*	Drug BCD ratio	% drug content in complex
1	1:1	36.04 ± 0.83
2	1:2	75.62 ± 0.49
3	1:3	26.34 ± 0.93

*Results are the mean of 3 observations ± SD

On the basis of these observations Drug BCD ratio 1:2 was finalized for further study.

Preparation of Lornoxicam Fast Dissolving Film

Water is heated to 80^{O}C and then 25 ml is taken in a beaker. To this 2 gms of HPMC is added under continues stirring for 10 min and keep it aside for 10hrs to get viscous lump.To this lump again add 8gms of purified water and 5gms of IPA under stirring for 2hrs . And then add SLS and Mannitol for 10min. Then add the remaining excipients one by one under continuous stirring for 30min.Keep it aside for 10hrs then pour into petriplate in the form of film and allow the film for drying at 80^{0}C for 15min. Cut the desired size and evaluate the films for physical and chemical properties. The composition of films are mentioned in Table no. 2

Table no 2 : Composition for fast dissolving film of lornoxicam

Ingredients mg/film	F1	F2	F3	F4	F5	F6	F7
Lornoxicam	8	8	8	8	8	8	8
SLS	15	15	15	15	15	15	15
Mannitol	10	10	10	10	10	10	10
HPMC E5	20	20	20	20	20	20	20
Glycerol	10	10	10	10	10	10	10
Citric acid	10	10	10	10	10	10	10
aspartame	5	5	5	5	5	5	5
Tartazine	0.1	0.1	0.1	0.1	0.1	0.1	0.1
SSG	-	5	10	15	-	-	-
CCS	-	-	-	-	5	10	15
Purified water	80	80	80	80	80	80	80
IPA	50	50	50	50	50	50	50

Evaluation of Oral Dispersible Films [5,6,7]

1. Physical appearance: All the prepared Films were visually inspected for colour, clarity, flexibility and smoothness. The physical and chemical parameters of different formulations of lornoxicam from F1 to F7 studied are represented in Table 3.

2. Thickness Uniformity: The thickness of the formulated film was measured at 3 different places and average thickness of three readings was calculated.

3. Weight Uniformity: For each formulation, three randomly selected films were used. For weight variation test 3 films from each batch were weighed individually and the average weight was calculated.

4. Folding endurance: The folding endurance was measured manually for the prepared films. A strip film (3X3 cm) was cut and repeatedly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking/cracking gave the value of folding endurance.

5. Percentage moisture absorption: The films were weighed accurately and placed in the desiccators containing 100ml of saturated solution of potassium chloride, which maintains 80-90% RH. After 3days, the films were taken out and weighed. The study performed at room temperature. The percentage moisture absorption was calculated using the formula

$$\text{Moisture absorption} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

1) **Percentage moisture loss:** The films were weighed accurately and kept in a dessicator containing anhydrous calcium chloride. After 3days the films were taken out and weighed. The moisture loss was calculated using the formula:

$$\%\ \text{Moisture loss} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

6. Drug content uniformity of films: The films (1cm2)were cut and added to a beaker containing 100ml of phosphate buffered saline of pH 6.8. The medium was stirred with magnetic bead. The contents were filtered using Whatmann filter paper and the filtrate was examined for the drug content against the reference solution consisting of placebo films at 375nm spectrophotometrically. The experiment was repeated to validate the result.

7. In vitro drug release studies: The In vitro drug dissolution of films were performed using Phosphate buffer pH6.8 at 37±50C. 5ml of Sample was withdrawn periodically for every 10min upto 50min by replacing with dissolution medium and these samples were again diluted and examined spectrophometrically at 375nm.

RESULTS AND DISCUSSION

1) Physical appearance: All the prepared films were transparent, smooth, uniform and flexible.

2) Thickness Uniformity: The thickness of the formulated film were varies from 19.45 to 25.95mm. Low standard deviation values ensured uniformity of the patches.

3) Weight Uniformity: The weights ranged between 119.5 to 126.1 mg as mentioned in **Table No:3**

4) Folding endurance: The folding endurance was found to be >100 which was sufficient **Table No:3**

5) Percentage moisture absorption: The films were found to be it increases with increasing concentration of hydrophilic polymers.

6) Drug content uniformity of films: Drug content was found to be 89.56 % to 97.65 % as mentioned in **Table No.3**.

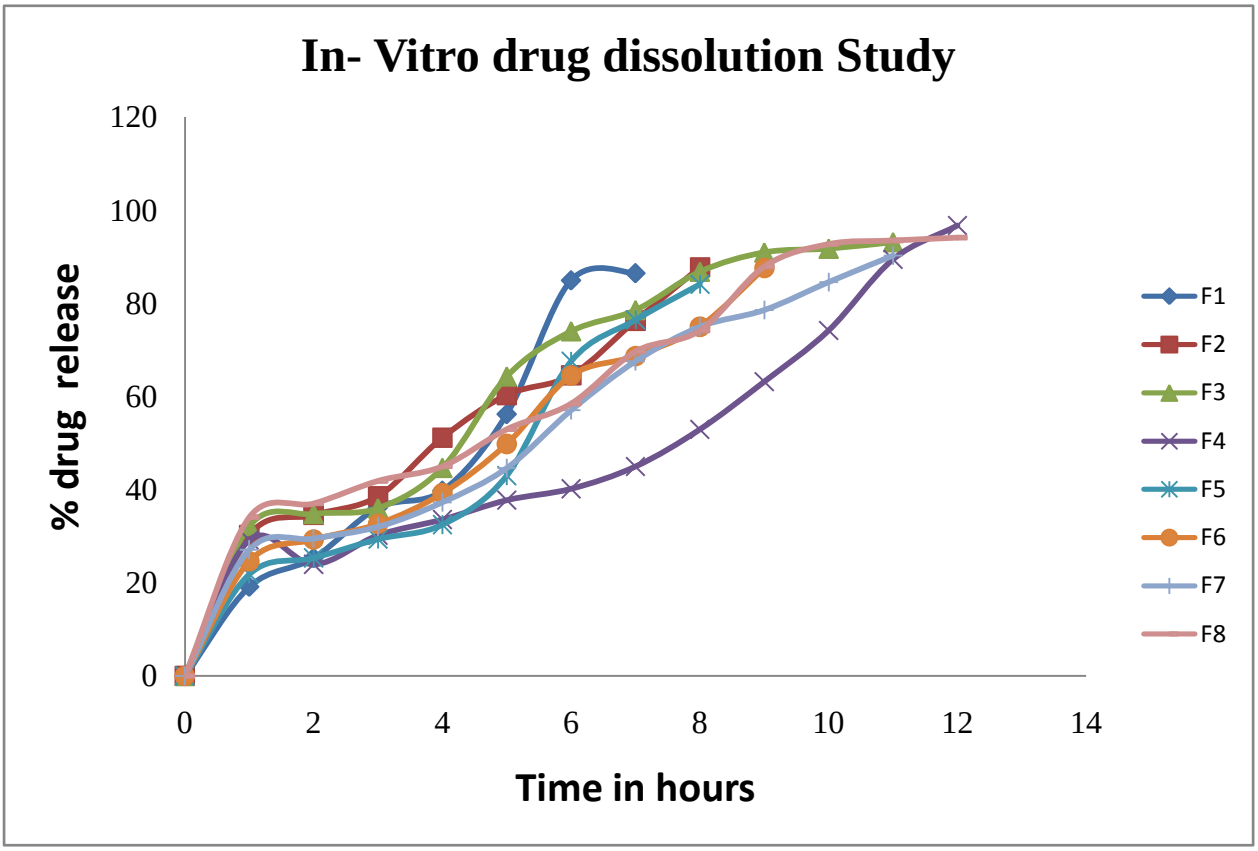
Table No:3 Thickness, mean weight(mg), drug content(mg),% HYDRATION, %moisture loss & surface pH,Folding endurance,disintegration time

Formulation	Thickness	Mean weight(mg)	Drug content(%)	%hydration ratio	% moisture loss	Surface pH	Folding endurance	Disintegration time
F1	23.65	121.1	94.23	0.645	2.543	6.65	143	31
F2	24.39	125.1	94.26	0.689	1.111	6.63	156	24
F3	24.21	126.1	96.78	0.754	1.324	6.45	121	28
F4	19.45	124.2	97.65	0.80	2.324	6.34	161	26
F5	22.87	119.5	91.78	0.611	1.198	6.81	148	36
F6	23.67	123.8	89.56	0.543	2.234	7.03	151	24
F7	25.95	121.8	91.34	0.463	2.234	6.61	158	28

7) In vitro drug release studies: The result indicated that the release of drug from films having HPMC E5 shows better dissolution. The cumulative percentage of immediate release Oral Dispesible Film was 93.71 % in 30 min from formulation F4 (Table No 4)

Table no.4 In vitro Percent drug release profile of formulations

Time (sec)	% drug release							
	F1	F2	F3	F4	F5	F6	F7	Marketed
5	57.52	56.60	58.45	59.38	46.32	49.34	42.45	48.89
10	63.09	62.16	64.94	64.92	52.19	55.76	47.67	58.09
15	69.59	67.73	70.52	73.30	59.80	62.45	52.23	65.87
20	76.08	74.23	77.01	78.87	66.76	72.65	59.76	78.27
25	82.58	81.65	84.43	86.29	72.32	78.12	65.43	82.44
30	82.98	89.07	91.87	93.71	81.12	83.89	74.66	89.6



Graph No. 1 % drug release of all formulations

CONCLUSION

Inclusion complex of lornoxicam with beta cyclodextrin showed improve dissolution behavior pure drug which was prepared by kneading method. Result suggested that by complexing drug with beta cyclodextrin in 1:2 ratios marked with the bitter taste of drug. The fast dissolving film of lornoxicam was prepared by solvent casting method using HPMC. The prepared film was evaluated for different parameters and the result was found to be promising ensuring safe, bioequivalent, and effective dosage form.

From the result obtained, it was concluded that the formulation of fast dissolving film with F4 have better physical chemical properties with good dissolution property.

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