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FORMULATION AND EVALUATION OF FAST DISSOLVING ORAL FILM OF MELOXICAM

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Abstract: The oral route is most popular route for the administration of therapeutic agents because of the low cost of therapy and ease of administration. The most popular oral solid dosage forms are tablets and capsules. Many patients find it difficult to swallow tablets and hard gelatine capsules particularly paediatric and geriatric patients. To overcome these difficulties, several fast dissolving drug delivery systems have been developed. Recently, fast dissolving films are gaining interest as an alternative of fast dissolving tablets. Which quickly hydrated & dissolves when placed on the tongue to provide rapid local or systemic drug delivery without need of water. Meloxicam is water insoluble drug hence to make it solubilise it is formulated as drug-inclusion complex by using beta cyclodextrin in 1:1 ratio to enhance the solubility of the drug. The drug - inclusion complex were investigated for complex formation by FTIR, *in-vitro* dissolution and drug content. Meloxicam rapid dissolving films were prepared using different polymers like HPMC E5, PVA and polyox NF 10. PEG 400, glycerine and propylene glycol were used as plasticizers. The films were prepared by solvent casting technique. The 3^2 factorial design was applied for optimization of concentration of polymer PVA and plasticizer PEG 400. The prepared films were evaluated for various parameters related to delivery system like thickness, tensile strength, % elongation, folding endurance, disintegration time, drug content, *In vitro* release study and stability study. From design statistical analysis, the film (batch F6) with PVA (5%) and plasticizer PEG 400 (30%) was giving good disintegration time (51 sec), sufficient strength and high drug release (97.74%) and better %elongation. Thus, Meloxicam film was formulated giving fast relief in pain, inflammation & fever.

Keywords: Fast Dissolving Film, Meloxicam, PVA, PEG-400

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INTRODUCTION

FAST DISSOLVING DRUG DELIVERY SYSTEM

These dosage forms are intended to disintegrate, dissolve or release the drug in the oral cavity, where it has opportunity to be locally absorbed, in part or whole and alternatively may be swallowed and subsequently absorbed along the gastro-intestinal tract. Rapid dissolving drug delivery system are designed to meet the needs of special patients like geriatric, paediatric, mentally ill patients and dysphasic patients having difficulty in swallowing or chewing solid dosage forms.[13]

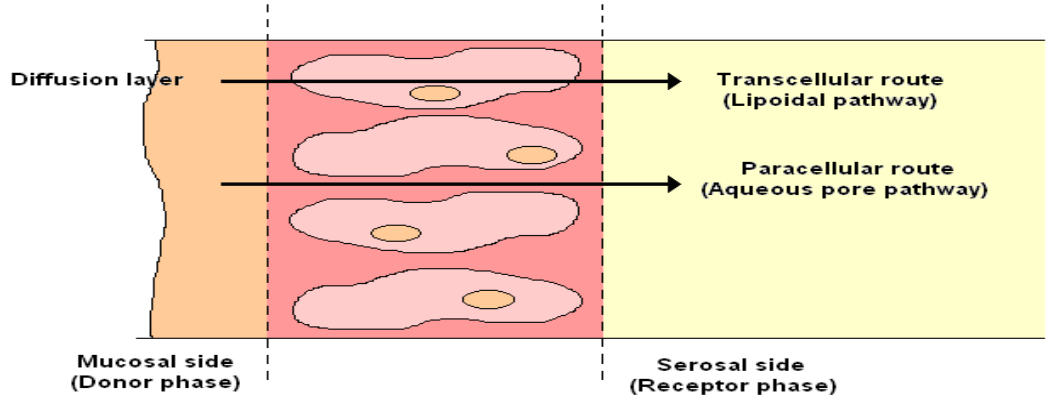

Figure 1: Drug absorption pathways across buccal mucosa

Classification of rapid dissolving technology[4]

For ease of description, fast dissolving technologies can be divided in to three broad groups:

1. Lyophilized systems,
2. Compressed tablet-based systems,
3. Thin film strips.

FAST DISSOLVING FILMS

Rapid dissolving film consists of fast dissolving polymer film embedded with drug. Which Quickly hydrated and dissolves when placed on the tongue or in the oral cavity (i.e., bucal, Palatal, gingival, lingualor sublingual) to provide rapid local or systemic drug delivery without need of water. The rapid dissolving film is also known as fast dissolving film, quick dissolving film, mouth dissolving film or oral thin film. Basically the rapid dissolving film can be consider as an ultra thin film of postage stamp size with an active agent or active pharmaceutical ingredient (API) and other excipients. The advantages of convenience of dosing and portability of rapid

dissolving film have led to wider acceptability of this dosage form by pediatric as well as geriatric population equally. The film reportedly incorporates soluble, insoluble or taste masked drug substance. The film is manufactured as a large sheet and then cut into individual dosage unit for packaging in a range of pharmaceutical acceptable formats. These films generally dissolve rapidly (within seconds), to release the active agents, but can be tailored to release the drug more slowly as well, depending upon their thickness, and selection of the polymer matrix.

Figure 2: Fast dissolving oral films

MATERIAL

Meloxicam was obtained from Cayman chemical. HPMC E5 was obtained from Dow chemicals, Pune. Poly vinyl alcohol was obtained from S.D.Fine chemicals, Mumbai. Polyox NF10 was obtained from Dow chemicals, Pune. PEG- 400, PG, Glycerol was obtained from ACME chemicals, Bombay. Aspartame, Citric acid was obtained from Himedia pvt.ltd, Bombay. Flavour was obtained from ACME chemicals, Bombay.

METHOD

Solvent casting method

In solvent casting method water soluble polymers are dissolved in water and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally casted in to the Petri plate dried and cut in to uniform dimensions

FACTORIAL DESIGN FORMULATIONS

For formulation of medicated films, the required amount of drug was added in prepared polymeric solution containing plasticizer and stirred on magnetic stirrer. To that solution calculated quantity of 10 mg citric acid, 15 mg aspartame, and 0.5 mg orange flavor were added and stirred. This solution was finally poured into the petridish. The total amount of drug added in all formulations was sufficient to produce the film containing 5 mg of drug/4cm^2.

Table 1. Composition of Factorial Design Formulations of Meloxicam

Batch No.	Drug: Inclusion Complex (mg)	PVA (%w/w)	PEG 400 (%w/w of dry polymer)	Citric Acid (mg)	Aspartame (mg)	Flavour (ml)	Water (ml)
F1	526.94	3%	20%	10	15	0.5	10
F2	526.94	4%	20%	10	15	0.5	10
F3	526.94	5%	20%	10	15	0.5	10
F4	526.94	3%	30%	10	15	0.5	10
F5	526.94	4%	30%	10	15	0.5	10
F6	526.94	5%	30%	10	15	0.5	10
F7	526.94	3%	40%	10	15	0.5	10
F8	526.94	4%	40%	10	15	0.5	10
F9	526.94	5%	40%	10	15	0.5	10

EVALUATION OF FACTORIAL DESIGN FORMULATIONS (F1 TO F9)

Table 2: Physicochemical Evaluation of Fast Dissolving Film of Meloxicam

Batch No.	Thickness* (mm)	Tensile* Strength (gm/cm^2)	% Elongation*	Folding Endurance*	Disintegration Time* (sec)
F1	0.109±0.06	324.00±2.53	6.1±2.09	102±1.52	35±2.65
F2	0.114±0.02	351.33±3.36	6.4±2.39	129±2.15	39±3.21
F3	0.125±0.03	388.41±1.55	7.8±2.52	147±3.52	55±5.13
F4	0.107±0.01	340.67±2.74	6.5±2.12	124±3.18	31±4.31
F5	0.116±0.03	374.45±3.53	7.1±1.82	131±2.53	45±5.26
F6	**0.127±0.05**	**411.66±2.15**	**8.0±1.11**	**147±2.08**	**51±5.15**
F7	0.111±0.03	365.32±2.73	7.3±1.87	121±3.68	42±3.41
F8	0.115±0.02	390.53±2.87	7.8±1.38	139±2.79	59±4.39
F9	0.126±0.04	438.92±3.22	8.4±2.33	143±2.53	73±6.78

*Values are means ± SD, (n=3).

Thickness

The results of thickness from various formulations (F1 to F9) are given in table 5.9. Thickness of all the films was in the range of 0.107±0.01 to 0.127±0.05 gm/cm^2 with very low values of standard deviation suggesting all films have appropriate thickness.

Tensile Strength

The results of tensile strength from various formulations (F1 to F9) are given in table 5.9. Tensile strength of all the films was in the range of 324±2.53 to 438±3.22 gm/cm^2 with very low values of standard deviation suggesting all films were having good mechanical strengths to withstand mechanical damage during, production and application.

% Elongation

The results of % elongation from various formulations (F1 to F9) are given in table 5.9.The results revealed that % elongation was in the range of 6.1±2.09 to 8.4±2.33. This represents the elasticity of the film. Increase in concentration of PVA results in enhancement of elasticity of films.

Folding Endurance

The results of folding endurance of various formulations (F1 to F9) are given in table 5.9 All the films were showing folding endurance in the range of 102±1.52 to 147±2.08. Results revealed that as the concentration of polymers increases folding endurance increases.

Disintegration Time

The results of disintegration time of various formulations (F1 to F9) are given in table 5.9.All the films were showing disintegration time in the range of 35±2.65 to 73±6.78. Results revealed that as the concentration of polymers increases disintegration time increases.

Table 3: Evaluation of prepared films

Batch No.	Drug content*	% moisture absorption	% moisture loss
F1	96.38 ± 1.30	1.70 ± 0.90	1.37 ± 0.58
F2	96.53 ± 1.41	1.66 ± 0.54	1.01 ± 0.15
F3	97.40 ± 0.45	1.99 ± 0.31	1.34 ± 0.92
F4	96.30 ± 0.34	1.60 ± 0.52	1.29 ± 0.50
F5	96.61 ± 1.41	1.58 ± 0.30	1.25 ± 0.37
F6	**97.55 ± 1.16**	**1.62 ± 0.25**	**1.22 ± 0.52**
F7	96.91 ± 0.49	1.76 ± 0.54	1.53 ± 0.51
F8	97.26 ± 1.18	2.04 ± 0.52	2.06 ± 0.14
F9	97.89 ± 1.27	2.00 ± 0.59	1.44 ± 0.58

*Values are means ± SD, (n=3).

Drug content

The results of drug content of various films are given in table 5.10. The results indicate that drug content of films were in the range of 96.30±0.34 to 97.89±1.27 %. The standard deviation values were very less suggesting that the drug was uniformly dispersed and the method adopted was accurate and reproducible.

% moisture absorption

The results of % moisture absorption of various films are given in table 5.10. The results indicate that % moisture absorption of films were in the range of 1.58±0.30 to 2.04±0.52. The standard deviation values were very less suggesting that the drug absorbed low moisture content.

% moisture loss

The results of % moisture loss of various films are given in table 5.10. The results indicate that % moisture loss of films were in the range of 1.01±0.15 to 2.06±0.14. The standard deviation values were very less suggesting that the drug lost low moisture content.

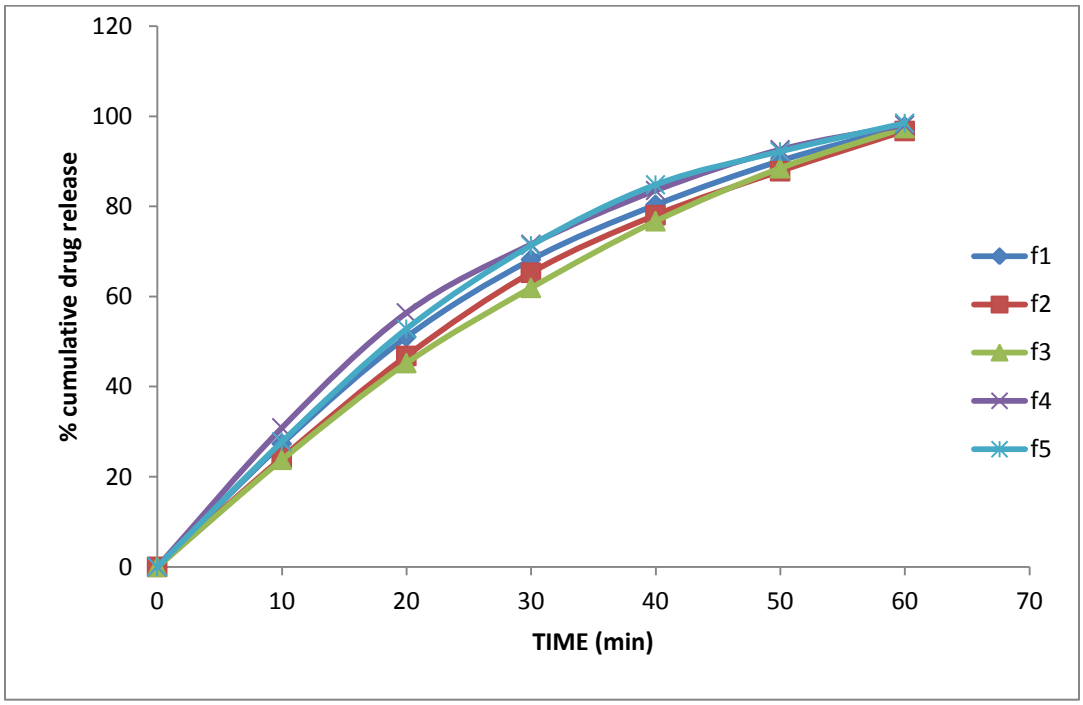

Fig. 3: *In vitro* dissolution of Meloxicam of formulations F1 to F5

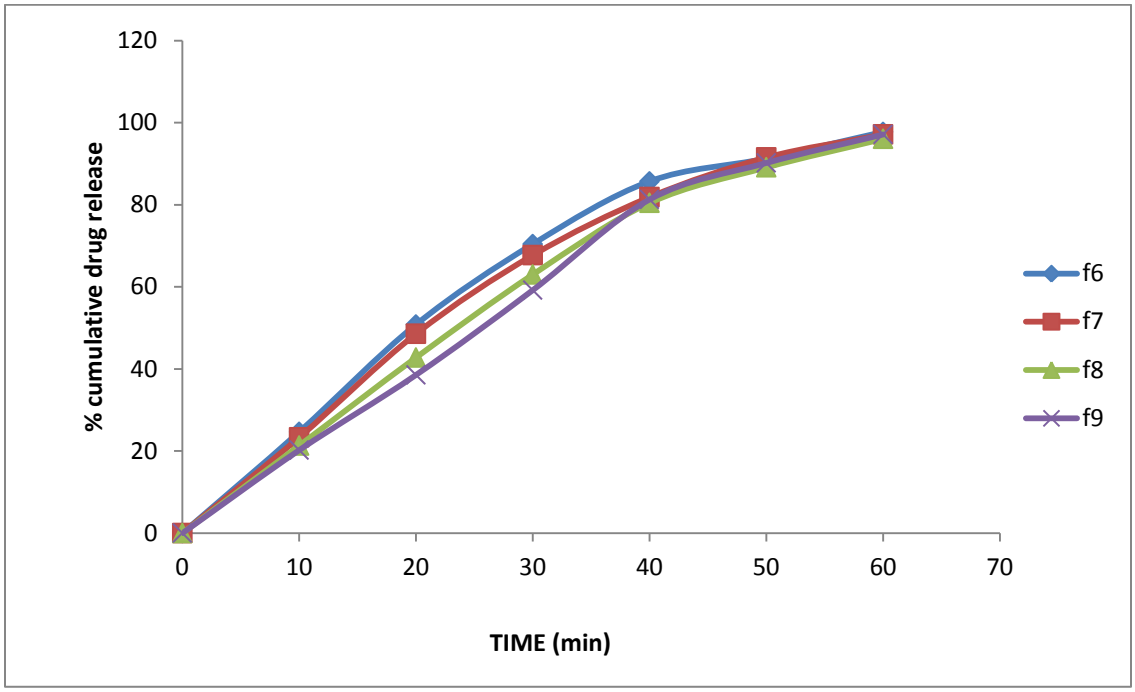

Fig. 4: *In vitro* dissolution of Meloxicam of formulations F6 to F9

RESULTS AND DISCUSSION

RESULTS

The purpose of the research was to develop a rapid dissolving films of Meloxicam. Meloxicam is a Nonsteroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic and antipyretic activities. Meloxicam is used for the treatment of arthritis & osteoarthritis. The prepared fast dissolving oral film will have an efficient bioavailability & will give fast onset of action for treatment of Arthritis. An attractive dosage form like rapid dissolving films can be formulated to increase the patient compliance. Moreover, rapid dissolving films have various advantages over conventional dosage forms like: Greater dissolution due to larger surface area, More patient compliance, No risk of chocking, Attractive in appearance and elimination of first pass metabolism. They are innovative and promising form for the patient having difficulties in swallowing tablet.

The solubility of the drug Meloxicam was firstly improved by preparing an inclusion complex of drug with beta cyclodextrin using kneading method. For the selection of optimum ratio of drug and beta cyclodextrin saturation solubility study was performed. From the results 1:1 ratio was selected as a optimum ratio. Further the complex was evaluated to check whether the complex has been formed or not.

After the formation of complex, the selection of film forming polymer was done. For this the blank polymeric films were prepared using different polymers such as HPMC E_5, PVA and polyox NF 10 by solvent casting method. PEG 400, glycerin and propylene glycol were used as plasticizers. Then blank polymeric films were evaluated for different physicochemical parameters like uniformity of thickness, disintegration time, tensile strength, % elongation, folding endurance, %cumulative drug release, %moisture loss, %moisture absorbed and % drug content. PVA and PEG-400 was selected as a film forming polymer and plasticizer respectively.

Statistical analysis of the factorial design formulations was performed by multiple regression analysis using Microsoft Excel 2007. The results of multiple regression analysis indicate that, for obtaining rapid dissolving films; optimum amount of PVA and PEG-400 should be used. A surface response plots and contour plots were also presented to graphically represent the effect of the independent variables on disintegration time, %cumulative drug release, %elongation and tensile strength. The validity of a generated mathematical model was tested by preparing a checkpoint formulation.

Among all the formulations, F6 was selected as a promising formulation on the basis of the disintegration time, %cumulative drug release, %elongation and tensile strength study and all other physicochemical parameters. Promising formulation F6 was subjected to stability study for 30 days and the results obtained revealed that films were stable for a period of 30 days.

CONCLUSION

The formulation F6 satisfied all pharmaceutical parameters of rapid dissolving films and appears to be promising would be able to offer benefits such as rapid drug release, good disintegration time, tensile strength and promising %elongation and thereby may help to improve the bioavailability of drug.

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