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FORMULATION AND *INVITRO* EVALUATION OF MOUTH DISSOLVING FILMS OF DICLOFENAC SODIUM USING SOLVENT CASTING TECHNIQUE

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ABSTRACT

Fast dissolving drug delivery systems such as mouth dissolving films (MDF) are novel dosage forms that disintegrate or dissolve within the oral cavity. These offer a convenient way of dosing medications, not only to special population groups with swallowing difficulties such as children and the elderly, but also to the general population. In the present study, mouth dissolving thin films of Diclofenac Sodium by solvent casting method using polymer hydroxyl propyl methyl cellulose and Plasticizer PEG4000are prepared and evaluated. Of all the formulations, MDF 3 shows best results. Formulation MDF3 is optimized with low concentration of polymers. Formulation MDF3 shows 100% drug release within 3min which is very less than other formulations.

Keywords: Mouth dissolving films, Buccal, solvent casting, diclofenac sodium and HPMC.

INTRODUCTION

Despite tremendous advancement in the drug delivery system, oral route is the most preferred route of administration and tablet and capsules are most preferred dosage form, but now they experienced several limitations like chocking and swelling discomforts in the geriatric and pediatric patients. Among the plethora of avenues explored oral strips gain more attention as it emerging news platform for geriatric and pediatric patients[1].

Fast dissolving drug delivery system (FDDS) was introduced in late 1970 as the alternative to conventional tablet, capsule and syrups especially for geriatric and pediatric patients suffering from the dysphasia problem. Fast solving films are solid dosage form which disintegrates rapidly in oral cavity without the need of water. Some problems are associated with the oral fast dissolving films like they are sometime difficult to carry, storing and handling (friability and fragility), these are prepared using the expensive lyophilisation method. To overcome these problems oral films were developed, which are very popular now a days[2,3].

The concept of oral film was come from confectionary industry. Oral films are the recent ultra thin novel formulation of postage stamp size which contains active pharmaceutical ingredient and excipients. Efficacy of API is improved as it dissolves in the oral cavity[4,5,6].

Oral films disintegrate rapidly within seconds when it comes contact with saliva without need of water. Oral fast dissolving films are useful for the patients suffering from the geriatric and pediatric patients and also for the patients suffering from the emesis, diarrhea, allergic attacks, cough, mental disorder and bedridden patients etc.

Oral films are used for the local effects like local anesthetics for oral ulcers, toothaches, cold scars and teething. Generally the shelf life of film is 2-3 years it depends on the active pharmaceutical ingredient is added to the film

but films are very sensitive to environmental moisture. An estimated 35% of the general population , and an additional 30-40% of elderly institutionalized patients and 1822% of all persons in long term care facilities, suffer from dysphagia, this disorder is associated with the many medical conditions including stroke, Parkinson's and other neurological disorders.

One study shows that 26% of 1576 patients experienced difficulty in swallowing tablets, the most common complaint was tablets size, followed by surface, form and taste. The problem of swallowing tablets was more evident in geriatric and pediatrics, as well as travelling patients who may not have ready access to water.

Salivary gland is present in the oral cavity which secretes saliva. Three salivary glands are present in the oral cavity i.e. parotid, submandibular and sublingual glands. Saliva is relatively less viscous as compared to gastro-intestinal fluids. Saliva is mainly water which contains 1% organic and inorganic material. Saliva is a weak buffer and its pH ranges from 5.5-7 .The total volume of saliva secreted from the salivary gland is 0.5-2 liters and it is the amount of saliva enough to hydrate oral mucosal dosage form.

Advantages of Mouth Dissolving Films[7,8]

This dosage form has some distinct advantages over other oral formulations such as-

1. Availability of larger surface area that leads to rapid disintegration and dissolution in the oral cavity.
2. Since the films are flexible they are not as fragile as most of the ODTs. Hence, there is ease of transportation and during consumer handling and storage.
3. As compared to the syrup formulations, precision in the administered dose is from each of the strips.
4. MDFs offer fast, accurate dosing in a safe, efficacious format that is convenient and portable, without water.
5. The oral or buccal mucosa being highly vascularized, drugs can be absorbed directly and can enter the systemic circulation without undergoing first pass hepatic metabolism.
6. Since the first pass effect can be avoided, there can be reduction in the dose which can lead to reduction in the side effects.
7. MDFs are typically size of postage stamp and disintegrate on a patient tongue in a matter of seconds for rapid release of AP (Table 1: Composition of different films).

Mouth Dissolving Films are typically the size of a postage stamp and disintegrate on a patient's tongue in a matter of seconds for the rapid release of one or more APIs.

By passing the first pass effect leads to reduction of dose which can lead to reduction inside effects associated with the molecules[2,3,4].

MATERIALS AND METHODS

Diclofenac Sodium was obtained as a gift sample from FDC Ltd, Goa. Polyethylene Glycol (PEG), hydroxypropylmethylcellulose (HPMC 15 cps and 50 cps) were procured from CDH Laboratories, New Delhi. All other chemicals used were of analytical grade. All other chemicals used were of analytical grade.

General method of formulation of mouth dissolving films

Following processes are generally used to prepare mouth dissolving film: hot melt extrusion, solid dispersion, rolling, semisolid casting and solvent casting. In the present study, mouth dissolving films of paracetamol were prepared by solvent casting method, which involved the following steps: preparation of casting solution (containing drug, polymer, plasticizer, sweetener and flavor), deaeration of the solution, transfer of appropriate volume of solution into a mould, drying the casting solution, cutting the final dosage form into strips (size 2x3 cm) to contain the desired amount of drug (125mg), packaging and storage. Different formulations were developed by varying polymer (hydroxylpropyl methylcellulose) and plasticizer (glycerol) concentrations. Sweetening and flavoring agents were added to make the formulation palatable. The films were evaluated for thickness, folding endurance, weight variation, disintegration time, dissolution time and drug content.

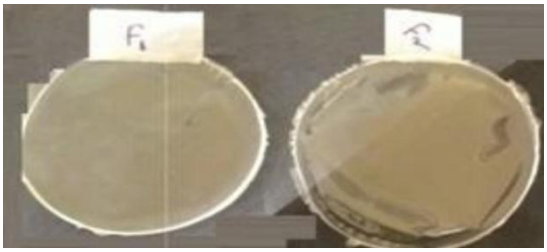

Fig. 1: Mouth dissolving films of diclofenac sodium

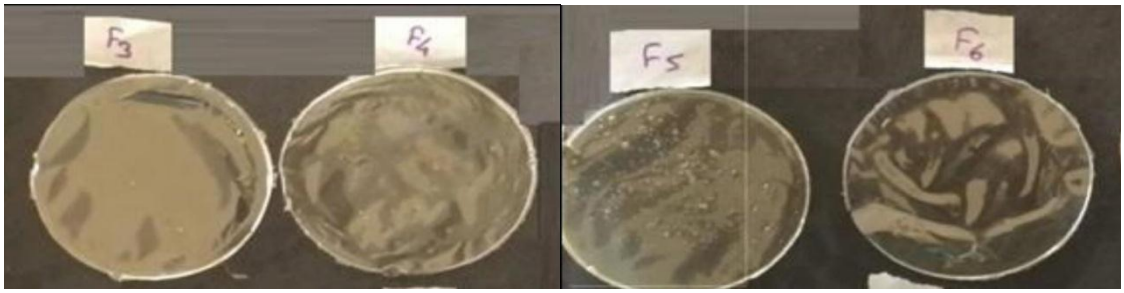

Fig. 2: Films

Evaluation of Films

Standard curve of Diclofenac

Procedure

100 mg of diclofenac (dfs) was dissolved in 10 mL methanol and volume was made upto100mL with the distilled water. 10 mL of the above solution was diluted up to 100 ml with distilled water. From this solution, 1 ml was taken and volume was made up the100ml (1µg/ml). Then by serial dilution, solutions with concentrations 2µg/ml, 4µg/ml, 6µg/ml, 8µg/ml and 10µg/ml were prepared. Absorbance was measured on a Shimadzu Double Beam Spectrophotometer (UV1601) at 275nm.

Weight variation of the film

2x3 cm film was cut from different locations in the caste film. The weight of each film strip was taken and the weight variation was calculated.

Disintegration time

Disintegration time study was slightly modified to mimic the *in-vitroand in-vivo* conditions. For the study, film as per the dimensions (2 x3 cm) required for dose delivery was placed in a basket containing 900mL distilled water. Time required for the film to break and disintegrate was noted as *in-vitro* disintegration time.

***In-vitro* dissolution studies**

The *in-vitro* dissolution studies were conducted using pH 6.8phosphate buffer (900 mL). The dissolution studies were carried outusing six basket dissolution dissolution apparatus at 37 ± 0.5 °C and at 50 rpm. Each film with dimension (2 x 3 cm) was placed on a stainless steel basket. The film sample placed on the sieve was submerged into dissolution media. Samples were withdrawn at 5, 10, 15, 20, 25 and 30min. time intervals and filtered through 0.45µm Whatman filter paper and were analyzed spectrophotometrically at 276 nm. To maintain the volume, an equal volume of fresh dissolution medium maintained at same temperature was added after withdrawing samples. The absorbance values were converted to concentration using standard calibration curve previously obtained by experiment.

Results

Standard curve of PC Mat different concentrations a concentration dependent increase in absorbance was observed in agreement with Beer Lambert Law (Table 1). The obtained standard curve is shown in Fig 2.

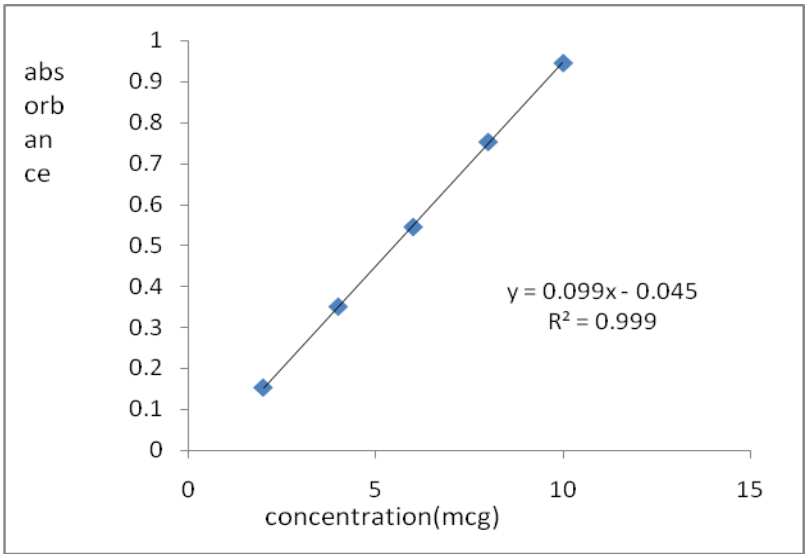

Fig . 3

Table 1: Composition of different films

Formulation code	Drug (mg)	HPMC 15cps (mg)	HPMC 50cps (mg)	PEG (mg)	Ethanol (ml)	Sucralose (mg)
MDF 1	0.36	1	-	0.08	15	0.03
MDF2	0.36	-	1	0.08	15	0.03
MDF3	0.36	1	-	0.08	15	0.03
MDF4	0.36	-	1	0.08	15	0.03
MDF5	0.36	0.5	-	0.08	15	0.03
MDF6	0.36	-	0.5	0.08	15	0.03

Table 2: Characterization parameters of different batches

S.no	Formulation code	weight variation (mg)	Dispersion time (min)
1.	MDF1	0.72	7
2.	MDF2	0.73	6
3.	MDF3	0.75	3
4.	MDF4	0.71	4
5.	MDF5	0.74	4
6.	MDF6	0.70	4

Table 3: In-vitro dissolution profile of films of diclofenac sodium

S.no	Time (min)	Percentage drug dissolved					
		MDF1	MDF2	MDF3	MDF4	MDF5	MDF6
1.	5	62	62	74.2	61.2	68	71
2.	10	75	78	91.3	66	76	78
3.	15	82	89	100	81	79	81
4.	20	91	95	100	96	89.8	91
5.	25	98	99	100	100	100	96
6.	30	98	99	100	100	100	100

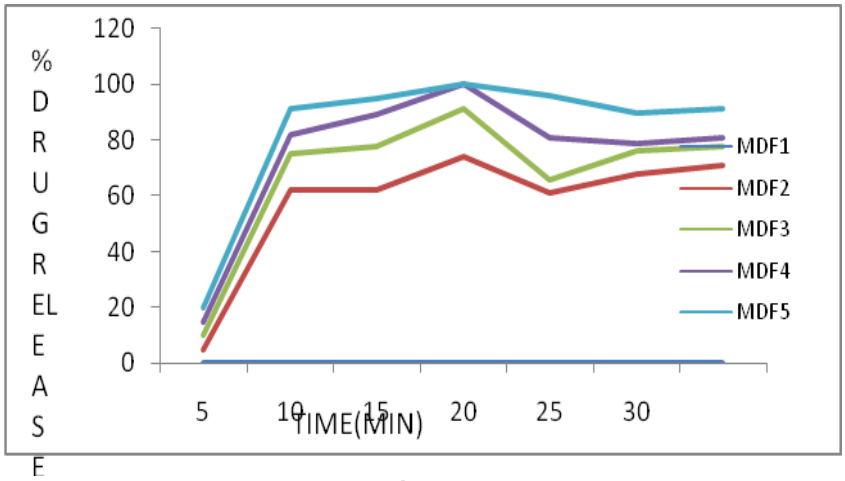

Fig. 4:

CONCLUSION

In the present study, mouth dissolving thin films of Diclofenac Sodium by solvent casting method using polymer hydroxyl propyl methyl cellulose and Plasticizer PEG4000 are prepared and evaluated. Of all the formulations, MDF 3 shows best results. Formulation MDF3 is optimized with low concentration of polymers. Formulation MDF3 shows 100% drug release within 3min which is very less than other formulations.

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