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Original Article

Formulation and Evaluation of Domperidone Fast Dissolving Film by Using Different Polymers

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ABSTRACT

The present study deals with the investigation carried out on developing a fast dissolving delivery system releasing Domperidone concomitantly in stomach for treating vomiting and motion sickness. Domperidone FDOF was prepared by solvent casting principle. Different concentration of film forming polymer i.e. Domperidone with and without solubilising agent tween 80 was used to formulate FD of Domperidone. The films formulated by incorporating a solubilising agent i.e. tween 80 had better. Korsmeyer-peppas model was found to be best fit kinetic in which all formulation showed good linearity (R^2: 0.906 to 0.989), with slope (n) values ranging from 0.655 to 0.981.In Korsmeyer-Peppas model, 'n' is the release exponent indicative of mechanism of drug release. The 'n' values ranged from 0.5-1.0 indicate Anomalous transport (non-fickian) diffusion where drug release is both diffusion and swelling controlled.

Key Point: FDOF, Korsmeyer-Peppas Model, Polymers, Solublising Agent.

1. INTRODUCTION

Oral films disintegrate rapidly within seconds when it comes in contact with saliva without the need of water. Oral fast dissolving films are useful for the geriatric and paediatric patients and also for the patients suffering from emesis, diarrhoea, allergic attacks, cough, mental disorder, bedridden patients etc. Oral films are also used for local effects like local anaesthetics for oral ulcers, toothaches, cold scars and teething. [1]

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1.1 Fast dissolving films

However, the fear of taking solid tablets and the risk of choking for certain patient population still exist despite their short dissolution/disintegration time. Recent development in novel drug delivery system aims to enhance safety and efficacy of drug molecules by formulating a convenient dosage form for administration. One such approach is rapidly dissolving film. It consists of a very thin oral strip, which releases the active ingredient immediately after uptake into the oral cavity. Rapid film combines all the advantages of tablets (precise dosage, easy application) with those of liquid dosage forms (easy swallowing, rapid bioavailability)**.** The delivery system is simply placed on a patient's tongue or any oral mucosal tissue. Instantly wet by saliva, the film rapidly hydrates and dissolves to release the medication for oromucosal absorption. [2, 3]

Salient features of melt in mouth films

- The drug to be incorporated should have low dose up to 40 mg.
- The drugs with smaller and moderate molecular weight are preferable.
- The drug should have good stability and solubility in water as well as in saliva.
- It should be partially unionized at the pH of oral cavity.
- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.

Advantages of fast dissolving film

- Oral dissolving films can be administered without water, anywhere, any time.
- Due to the presence of larger surface area, films provide rapid disintegrating and dissolution in the oral cavity.
- Oral dissolving films are flexible and portable in nature so they provide ease in transportation.
- Suitability for geriatric and pediatric patients, who experience difficulties in swallowing mentally ill, the developmentally disable and the patients who are un-cooperative, or are on reduced liquid intake plans or are nauseated.
- Beneficial in cases such as motion sickness, acute pain, suede episodes of allergic attack or coughing, where an ultra rapid onset of action required.
- Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.
- The sublingual and buccal delivery of a drug via thin film has the potential to improve the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament.

2. MATERIAL AND METHODS

Domperidone, Hydroxy propyl methyl cellulose, PEG 4000, Tween 80, Methanol, Glycerine these were gifted by respective industries such as Morpan Pharma, and Loba Chemicals Mumbai. Sonicator used for mixing of polymers and drug. All the formulations of Domperidone FDOF displayed optimum folding endurance above 100 folds, which indicate the formulation prepared can withstand sufficient rough handling during transportation and handling of the formulation. The folding endurance was measured manually, films were folded 125 times maximum in Formulation F4 and if the film shows any cracks it was taken as end point. The folding endurance was better in F4 formulations.

Fig 1: FDOF of Domperidone

2.1 Dissolving Time

The disintegration test performed using Petridis method reviled that F7 disintegrated faster in 10 sec whereas F4 disintegrated in 18 sec. The formulation F5, F6 and F8 disintegrated in 13, 12 and 14 sec respectively. Formulation F1, F2 and F3 disintegrated in 15, 16 and 17 sec respectively. [4, 5]

Table 1: Dissolving Time

Formulation code	Time (Sec)
F1	15±3.51
F2	16±3.06
F3	17±3.16
F4	18±3.61
F5	13±2.51
F6	12±3.06
F7	10±2.53
F8	14±3.17

2.2 Drug content Estimation

The drug content of Domperidone FDOF showed that all the formulations were containing Domperidone in the range of 89.37 to 98.09%.

Table 2: Drug content Estimation

Formulation code	%drug content in 2.5 × 2.5 cm
F1	89.37±0.962
F2	97.06±1.272
F3	93.78±1.442
F4	95.91±0.481
F5	90.89±1.733
F6	97.54±0.481
F7	92.56±0.470
F8	98.09±1.721

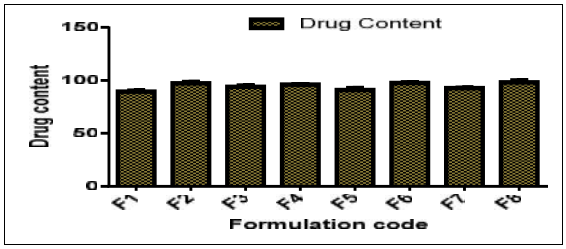

Fig 2: Drug content estimation study of formulated batches

2.3 Moisture content

Moisture loss is defined as the quantity of moisture transmitted through unit area of film in unit time. The moisture content study gives an idea about films stability nature and ability of films to withstand its physicochemical properties under normal conditions.It also gives idea about hydrophilicity of film formulations. The obtained values are almost uniform and ranges from 1.37±0.48% to 3.13±0.53%. F8 formulation showed high % moisture content while F1 and F2 formulations showed low % moisture content .Higher concentration of Polymers in F8 may be the reason for higher percentage of moisture content. [6, 7]

Table 3: Moisture content estimation

Formulation code	Moisture content (%)
F1	1.37±0.48
F2	1.88±0.50
F3	2.37±0.37
F4	2.88±0.57
F5	2.21±0.08
F6	2.50±0.34
F7	2.56±0.43
F8	3.13±0.53

Value represent mean±SD where n=3

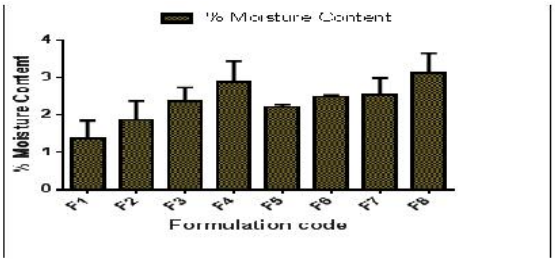

Fig 3: Moisture content study of formulated batches

2.4 In-vitro release study

The dissolution studies were conducted using phosphate buffer pH 6.8.Each film strip (containing drug equivalent to 5 mg) was then submerged into the dissolution medium. The dissolution study was carried out using dissolution test apparatus USP type-II at 37˚C, at 50 rpm, using 900 ml phosphate buffer (pH 6.8) as dissolution medium. Test samples were withdrawn at different time intervals and analyzed

spectrophotometrically at 284 nm. The absorbance values were transformed into concentration using standard graphic. *In vitro* drug dissolution study of the Domperidone film was conducted in phosphate buffer 6.8 solution.The rate and extent of drug release from the dissolving film was found to be of the order F1< F2< F5<F3<F4< F6< F8<F7. The drug release was found to be slower in formulations with increasing polymers concentration. The Batch F1 showed 94.68 % drug release within 5 min in phosphate buffer 6.8. Batch F1 showed minimum 94.68 % drug release within 5 min and F7 showed maximum drug release within 5min.F7 showed maximum 98.52 % drug release within 5 min. [8-10]

Table 4: Cumulative drug release from formulations

Sr. No.	Time (min)	% Cumulative drug release							
		F1	F2	F3	F4	F5	F6	F7	F8
1	0	0	0	0	0	0	0	0	0
2	1	22.8±2.32	25.2±1.26	35.76±1.89	29.4±2.08	37.2±2.73	33.36±2.31	36±2.46	25.32±2.14
3	2	50.4±3.12	38.4±3.08	59.64±0.98	54.72±1.42	51.72±2.01	56.04±1.26	69.6±1.34	58.68±1.26
4	3	64.8±1.79	57.2±1.76	71.76±2.47	61.44±2.68	76.08±3.55	74.76±2.05	80.4±1.89	73.2±2.78
5	4	85.2±2.42	75.6±2.43	82.86±2.78	86.76±0.89	82.76±3.11	82.68±2.47	94.8±2.08	85.32±1.74
6	5	94.68±2.1	94.8±1.6	95.76±0.97	97.44±1.95	95.4±1.597	97.2±2.48	98.52±2.4	97.44±1.8

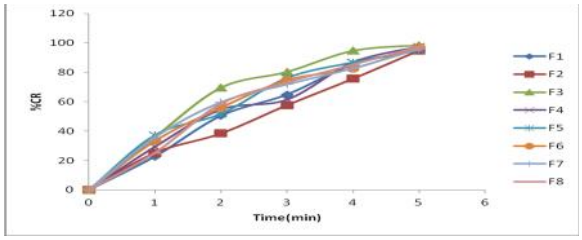

Fig 4: *In-vitro* release studies of formulated batches

Fig 5: First order release profile of Domperidone for all formulations

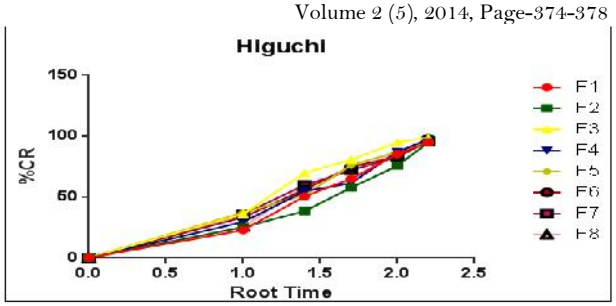

Fig 6: Higuchi release profile of Domperidone for all formulations

3. DISCUSSION

All the formulations are found to be in acceptable physical and dissolving properties. The shape, size, buoyancy, tensile strength, percent elongation and *in-vitro* release of batch F7 had good characteristics of an ideal dissolving formulation. Also the cumulative drug release of batch F7 was found to have good release characteristics with 36 % at 1 min and release upto 98.5 % in 5 min & also be concluded that presence of tween 80 increases the rapid release of Domperidone. Hence selected as an optimized formulation and the release kinetic graph. [11-14]

4. CONCLUSION

It can be concluded Domperidone FDOF with optimum physical appearance, disintegration and drug release can be formulated successfully by using HPMC Glycerine as film forming agent and tween 80 as a solubilising agent. Korsmeyer-peppas model was found to be best fit kinetic in which all formulation showed good linearity (R^2: 0.906 to 0.989), with slope (n) values ranging from 0.655 to 0.981.In Korsmeyer-Peppas model, 'n' is the release exponent indicative of mechanism of drug release. The 'n' value ranged from 0.5-1.0 indicates Anomalous transport (non-fickian) diffusion where drug release is both diffusion and swelling controlled.

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