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FORMULATION AND EVALUATION OF ORAL FAST DISINTEGRATING FILMS OF LORATIDINE

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ABSTRACT

The fast disintegrating oral films of Loratadine are prepared using HPMC E15cps, Eudragit and PVP individully and in combination of secondary polymers like MCC, PEG 400, in different ratios with suitable plasticizer like propylene glycol and sweetener like aspartame by solvent casting method. Among the formulations F1-F6, prepared using single polymer, the formulation F2 showed good drug release of 83.55±0.65% in 10 min and the In vitro disintegration time was found to be 59.33±4.04 sec. Among the formulations F7-F12, prepared using combination of the polymers, formulation F12 showed better drug release of 99.14±0.15 % in 6 min and the disintegration time was found to be 56.33±4.04 % sec. Formulation F12 is considered as optimum due to its good In-vitro dissolution and maximum drug release compare to other formulations. Along with F12, F9 showed good in vitro results.

Key words: Disintegration test, Loratadine, HPMC E15cps, EUDRAGIT, PVP.

INTRODUCTION

Novel oral drug delivery system dissolves or disperses quickly in few seconds after placement in the mouth without water can alleviate the problem of swallowing tablets. To overcome the problems associated with solid, liquid and parenteral dosage forms a novel oral dosage form is formulated now as fast dissolving oral films (FDOFs). FDOFs are the most advanced form of oral solid dosage form due to more flexibility and comfort. It improves the efficacy of active pharmaceutical ingredients (APIs) by dissolving with in minute in oral cavity after the contact with saliva without chewing or need of water for administration. Now-a-days pediatric and geriatric patients are facing the problem of dysphasia due to administration of monolithic solid dosage forms, which are also seen in the case of fast dissolving tablets considering the size of the tablets. Hence oral film drug delivery is proved to be better alternative in such cases [1].

The objective of our investigation is to the formulate and evaluate the fast dissolving film i.e. oral dissolving film technology (ODFTS) that can be administrated in the buccal cavity for a shorter period of time in Sec and gives better therapeutic action. ODFT offers an alternate platform for molecules that undergoes first pass metabolism [2].Most ODT products were formulated to dissolve in less than one minute when exposed to saliva to form a solution that could then be more easily swallowed [3].

METHODOLOGY

Matarials

Loratadine, Hydroxy propyl methyl cellulose, Propylene glycol, micro crystalline cellulose, Aspertame.

Preparation of Mouth Dissolving Films

The casting solutions were prepared by dissolving weighed quantities of polymers in required quantity of ethanol was taken in a beaker. The drug and aspartame were dissolved in required quantity of ethanol and added to the above polymer solution along with propylene glycol, and thoroughly mixed to form a homogeneous mixture. The volume was made up to 25 ml with ethanol. The beaker was covered with aluminum foil and solution was allowed to stand overnight for swelling of polymer and to remove air bubbles. The casting solution was poured in Petri plate and kept a side. The solution was casted on to a Petri dish and dried at 45^0C in hot air oven for 45 minutes.

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The film was carefully removed from the petri dish, and cut into square dimensions of 2 x 2 cm^2 per strip [4].

CHARACTERIZATION

Film Thickness

The thickness of 3 films of each formulation was performed by screw gauge at different position of the film and the average thickness was calculated.

Uniformity of weight

The film (4 cm^2) was cut at five different places in the cast film. The weight of each filmstrip was taken and the weight variation was calculated.

Uniformity of drug content

This parameter was determined by dissolving one film of dimension 2 × 2 cm containing 10 mg of Loratadine by homogenization in a mixture of 5 ml of ethyl alcohol and 100ml of simulated saliva of pH 6.75 for 30 min with continuous shaking. Then the solution was filtered and after suitable dilution with simulated salivary fluid, the absorbance was measured at 247.2 nm using a UV spectrophotometer and the drug content was calculated.

Folding endurance

The folding endurance is expressed as the number of folds (number of times the film is folded at the same place) required to break the specimen or to develop visible cracks.This also gives an indication of brittleness of the film. A strip of 2 × 2 cm (4 cm2) was subjected to folding endurance by folding the film at the same place repeatedly several times until a visible crack was observed, and the values were reported.

Surface pH

The film to be tested was placed in a petri dish and was moistened with 0.5 ml of distilled water and kept for 30s. pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and allowing equilibration for 1 min the average of three determinations for each formulation was done.

Tensile strength and % Elongation

This mechanical property was evaluated using the Instron universal testing instrument (Model F. 4026, Instron Ltd.,Japan) with a 5 kg load cell. Film strips in special dimension and free from air bubbles, physical imperfections were held between two clamps positioned at a distance of 3 cm. During measurement, the strips were pulled by the top clamps at the rate of 100 mm/min the force and elongation were measured when the film broke. Measurements were run in triplicate for eachfilm. Two mechanical properties, namely tensile strength and percentage elongation were computed for the evaluation of the film. Tensile strength is the maximum stress applied to a point at which the film specimen breaks and can be computed from the applied load at rupture as a mean of three measurements and the cross sectional area of the fractured film.

Disintegration test

Disintegration test was performed to ensure the disintegration of the film in water. One film from each formulation was introduced into one tube of disintegration apparatus IP. A disc was added into the tube the assembly was suspended ina beaker containing simulated saliva and the apparatus was operated until the film gets disintegrated. Test was performed in triplicate.

In vitro Dissolution studies

The simulated salivary fluid containing 2% ethanol after considering solubility factors of the drug was taken as the dissolution medium to determine the drug release. The dissolution profile of quick release films of Loratadine was carried out using USP type II (paddle apparatus) with 300 ml of simulated salivary fluid (pH 6.8) and dissolution medium maintained at 37± 0.5°C. The medium was stirred at100 rpm. Aliquots (5 ml) of the dissolution medium were withdrawn at 30 sec, 2min, 4min, 6min, 8min and 10min time interval and replacing the same amount with the fresh medium. Amount of drug in the withdrawn samples was determined by UV Spectrophotometer at 247.2 nm. Three trials were carried out of all the samples and the average value was taken. The percentage of drug dissolved at various time intervals was calculated and plotted against time [5].

Table 1. Composition of Loratadine containing Mouth dissolving films

FormulationCode	Polymers	HPMC E15 (mg)	Eudragit RL100 (mg)	PVP (mg)	MCC (mg)	PEG 400 (ml)	Propylene glycol (ml)	Aspartame (mg)
F1	HPMC E15 (1:4)	400	-	-	-	-	1	50
F2	HPMC E15 (1:6)	600	-	-	-	-	1	50
F3	Eudragit (1:4)	-	400	-	-		1	50
F4	Eudragit	-	600	-	-		1	50

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	(1:6)							
F5	PVP (1:4)	-	-	400	-		1	50
F6	PVP (1:6)	-	-	600	-		1	50
F7	HPMC+MCC (1:4:1)	400	-	-	100		1	50
F8	HPMC+MCC (1:3.5:1.5)	350	-	-	150		1	50
F9	HPMC+MCC (1:3:2)	300	-	-	100		1	50
F10	HPMC+PEG 400(1:4;1)	400	-	-	-	100	1	50
F11	HPMC+PEG 400 (1:3.5:1.5)	350	-	-	-	150	1	50
F12	HPMC+PEG 400 (1:3:2)	300	-	-	-	200	1	50

Table 2. Comparision of Evaluation parameters of formulations F1-F12

Formulation code	Thickness(mm)	Weight Variation (mg)	Drug Content (%)	Folding Endurance
F1	0.17±0.02	46.6±7.4	92.4±2.5	209.3±7.3
F2	0.19±0.02	48.2±7.5	94.0±2.0	212.3±2.5
F3	0.12±0.01	38.6±2.1	92±2	201.3±4.5
F4	0.11±0.026	40.8±3.4	92.05±5.7	205.3±3.5
F5	0.14±0.015	34.2±3.1	91.4±1.2	202.3±4.1
F6	0.12±0.015	35.6±3.8	91.8±1.0	200.3±3.2
F7	0.19±0.015	47.8±7.3	93.4±1.6	232.3±5.8
F8	0.19±0.01	48.8±7.4	93.4±0.7	232.6±5.5
F9	0.20±0.015	47.4±7.6	95.3±0.6	237.6±2.5
F10	0.19±0.005	50.6±6.9	97.1±1.05	246.6±4.1
F11	0.20±0.015	50.2±8.1	96.6±1.2	249.6±2.5
F12	0.2±0.01	51±6.8	98.65±0.5	251.6±2.0

Table 3. Comparison of Evaluation parameters of formulations F_1-F_{12}

Formulation Code	Surface pH	Disintegration time(Sec)	Tensile strength (M Pa)	Percent Elongation
F1	7.13±0.11	55.08±3.0	2.38±0.71	21.14±0.95
F2	7.13±0.05	59.33±4.04	3.75±0.11	21.8±1.2
F3	6.94±0.11	62.33±2.51	0.95±0.07	18.65±0.58
F4	7.006±0.02	72.3±2.5	1.06±0.16	19.93±0.65
F5	6.91±0.29	66.15±2.39	0.86±0.12	17.84±0.78
F6	7.18±0.59	67.01±2.02	1±0.04	18.41±0.52
F7	7.16±0.23	53.31±4.18	1.66±0.36	24.92±2.8
F8	7.18±0.06	55.41±5.81	1.98±0.05	25.68±1.26
F9	7.13±0.19	51.08±3.4	1.01±0.13	30.48±2.00
F10	7.17±0.10	55.66±6.02	2.10±0.1	39±1.95
F11	7.39±0.1	58.66±4.16	2.21±0.07	44.83±4.38
F12	7.36±0.15	56.33±4.04	2.05±0.18	53.33±4.00

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Table 4. Comparision of *in vitro* dissolution profiles of Formulations F_1-F_6

TIME	F1	F2	F3	F4	F5	F6
30(Sec)	29.28±0.37	26.62±0.23	12.79±0.25	19.38±0.28	11.49±0.32	16.72±0.23
2(Min)	35.70±0.38	35.61±0.43	20.05±0.50	31.18±0.49	25.58±0.40	29.58±0.37
4(Min)	40.64±0.58	46.78±0.50	27.21±0.40	35.51±0.48	29.92±0.42	35.07±0.42
6(Min)	59.19±0.71	59.19±0.15	35.4±0.48	42.40±0.50	35.84±0.38	41.93±0.44
8(Min)	68.45±0.76	69.30±0.91	43.7±0.45	46.66±0.54	44.47±0.56	48.83±0.51
10(Min)	75.81±0.80	83.55±0.65	51.83±0.55	58.36±0.63	49.96±0.45	51.9±0.59

Table 5. Comparision of *in vitro* dissolution profiles of Formulations F_6-F_{12}

TIME	F7	F8	F9	F10	F11	F12
30(Min)	46.85±0.3	55.67±0.4	60.23±0.20	55.40±0.40	60.46±0.15	72.5±0.10
2(Min)	53.09±0.2	65.46±0.2	69.41±0.15	68.61±0.25	80.24±0.10	86.1±0.20
4(Min)	60.16±0.3	72.53±0.25	80.17±0.47	82.52±0.35	89.69±0.20	94.5±0.25
6(Min)	70.08±0.2	80.61±0.20	90.19±0.18	92.54±0.15	96.76±0.25	99.14±0.15
8(Min)	78.03±0.3	87.55±0.20	93.04±0.25	99.57±0.15	99.11±0.30	
10(Min)	90.62±0.3	95.29±0.2	99.5±0.25			

Fig 1. Comparison of in vitro dissolution profiles of Formulations F1-F6

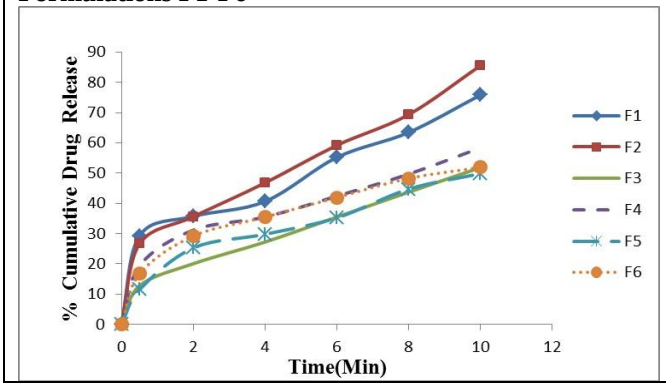
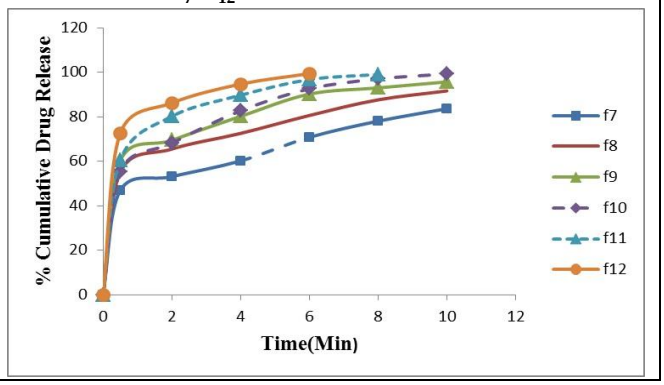


Fig 2. Comparison of in vitro dissolution profiles of Formulations F_7-F_{12}



RESULTS AND DISCUSSION

Twelve formulations of fast dissolving films of Loratadine were prepared by solvent casting method by using HPMC 15cps, PVP, Eudragit, MCC and PEG 400 as polymers. Propylene glycol was used as plasticizer and aspartame as sweetener. Effect of concentration ratio of polymers and nature of polymers was studied by preparing various formulations of fast dissolving films. In all these formulations a constant amount of drug (395 mg) was maintained. Each film (2 x2) cm^2 contains approximately 10mg of drug. In first six formulations, polymers were used in different concentrations 1:4 and 1:6. And remaining six formulations are combination of different concentrations of polymers and the concentration of other ingredients such as plasticizer and sweetener were kept constant.

The formulations F3, F4, F5 and F6 takes more time to disintegrate because of their poor film forming capacity. And in case of F7-F12 the disintegration time is decreased with increasing concentrations of HPMC, MCC, and PEG 400 as shown in table 2. When placed over the tongue, the film dissolved instantly. *In vitro* drug release study was carried out using USP dissolution apparatus, type II. Six formulations HPMC, PVP, EUDRAGIT films (F1, F2, F3, F4, F5 and F6) extent of drug release was greater in F1 and F2 films. When compared with F3, F4, F5, F6 and in reamainins formulations (F7, F8, and F9) the formulations F9 released the drug completly in 10 minutes. Among the formulations (F10 , F11 , F12) in F12 the drug was released completely within 6 minutes. Due to solubulization of drug within the PEG400 it leads to increase in the dissolution. All HPMC, PVP, EUDRAGIT, HPMC-PEG 400, HPMC-MCC (F1-F2) The order of drug release in each set of formulation can be given as F1< F2, F3 < F4, F5 < F6 < F7 < F8 < F9 < F10 <F11 < F12. Among all the formulations F12 and F9, showed better results in terms of percentage drug release and disintegration time.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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