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Design Development and Evaluation of oral thin films of Montelukast Sodium

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ABSTRACT

The present study reveals the use of Oral Thin Film (OTF) prepared by solvent casting technique. The prepared Montelukast loaded OTF can be used in emergency condition of severe asthmatic attacks. The comparison study by using Poly (ethylene) Oxide N-750 (PEO) and Hydroxy propyl methyl cellulose E15 (HPMCE15) as film forming polymer was performed. The results obtained for film disintegration and dissolution time tested orally correlated well with those obtained by the visual method. There was considerable reduction in film strength and increase in percent elongation of film with increase in glycerol content. The result showed that film containing PEO N-750 with 5 % glycerol showed better disintegration, dissolution and folding endurance when compared with film containing HPMCE15. Hence, the film containing PEO was used for further optimization where the optimized formulation (F2) depicted disintegration time of less than 6 sec, complete drug release within 8 min, percent elongation as 61.24 cm % and folding endurance more than 250 .

Keywords: Oral thin film (OTF); Montelukast sodium; PEO; HPMCE15

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INTRODUCTION

Availability of larger surface area in the film dosage form allows rapid wetting in the moist buccal environment that leads to rapid disintegrating and dissolution in the oral cavity. Rapid disintegration of film results in quick dissolution and rapid absorption, so that provide rapid onset of action. Due to rapid onset of action it may improve patient compliance and convenience. The difficulty encountered in swallowing and chocking tablets or capsules for yielders. Patients can take fast dissolving films at any time and any place as per their convenience [1-5]. Over the recent past, many of the research groups are focusing their research on this technology. The advantages of fast dissolving films are the administration to pediatric and geriatric patient population where the difficulty of swallowing larger oral dosage forms is eliminated[6]. This technology has been used for local action, rapid release products and for buccoadhesive systems that are retained for longer period in the oral cavity to release drug in controlled fashion[7]. Fast dissolving films offers an alternate platform for molecules that undergo first pass metabolism[8].

Asthma affects people of all ages, but it most often starts in childhood. In the United States, more than 20 million people are known to have asthma. Nearly 6.7 million of these people are children. But among adults, more women have the disease than men [9-10]. Some people develop asthma because of exposure to certain chemical irritants or industrial dusts in the workplace, this is called occupational asthma [11-12]. Montelukast sodium (M) 5, 6 is a leukotriene receptor antagonist (LTRA) used in treatment of asthma and to assuages symptoms of seasonal allergies. It is usually administered orally. Montelukast selectively antagonizes leukotriene D4 (LTD4) at the cysteinyl leukotriene receptor, CysLT1, in the human airway. Montelukast inhibits the actions of LTD4 at the CysLT1 receptor, preventing airway edema, smooth muscle contraction, and enhanced secretion of thick, viscous mucus [13]. Montelukast sodium is freely soluble in ethanol, methanol and water and practically insoluble in acetonitrile [14.]

The fast dissolving films can be used in emergency conditions such as emesis, hyperacidity, severe asthmatic attacks, etc. It could find a better application for patient compliance especially in children. Hence there is need to formulate fast dissolving delivery to control these severe conditions[15-16]. Poly (ethylene) Oxide is water-soluble polymer which provides binding, thickening, lubricity, water retention, and film formation benefits to deliver excellent performance in a variety of applications such as pharmaceuticals, mining, paper and cleaning products [17] There is need to formulate fast dissolving films using water soluble polymers for achieving rapid disintegration, good mouth feel and mechanical properties. Desired fast

disintegration and mechanical properties could be tailored with polyethylene oxide (PEO) and HPMCE15. Films had good mouth feel and no sticky feeling. Film strength of films containing PEO ranged between 3000 kg/m^2 to 17000 kg/m^2. Increase in glycerin content resulted in marked decrease in film strength [18-19].

MATERIALS AND METHODS

Materials

Montelukast sodium (Matrix Lab. Ltd., Nashik, Maharashtra, India.), Polyethylene oxide N-750 (Aldrich Chemicals, Mumbai, India), HPMCE15 (Merck Specialties Pvt. Ltd., Mumbai, India), Polyethylene glycol 400 (Loba chemie, Mumbai, India) and Glycerol (98%) (Loba chemie, Mumbai, India) were purchased for carrying out various experiments. All the chemicals used were of analytical grade.

Preparation of fast dissolving film

The fast dissolving films of montelukast sodium were prepared in the laboratory using the water soluble polymers PEO, HPMCE15 and PEG-400 or Glycerol (GLY) as plasticizer in appropriate proportion (Table 1A, 1B and 1C). Montelukast was dissolved in 20 ml methanol and sonicated for 2-3 minutes. In another side polyethylene oxide or HPMCE15 dissolved in distilled water (DW) by putting the solution on magnetic stirrer (rpm 30/min). Then both the solutions were mixed and plasticizer PEG 400 or GLY, and stirred well on magnetic stirrer (rpm 30/min). The above solution was allowed to stand for 30 min and degassed. The solution was casted in a petridish (diameter 8.8cm) and dried in hot air oven for 24 hrs. Then film was carefully removed from the petridish, checked for any imperfections and cut into the required size to deliver the equivalent dose (2 × 3 cm^2 per film).

Table 1A: Composition of different formulations containing PEO plasticized with glycerol

Components	Formulation											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
M (mg)	51	51	51	51	51	51	51	51	51	51	51	51
PEO (mg)	250	300	350	400	250	300	350	400	250	300	350	400
GLY (mg)	5	5	5	5	10	10	10	10	15	15	15	15
DW mL	10	10	10	10	10	10	10	10	10	10	10	10

Quantities of GLY are expressed in terms of %w/w of polymer (PEO)

Table 1B: Composition of different formulations containing HPMCE15 plasticized with PEG-400

Components	Formulation							
	G1	G2	G3	G4	G5	G6	G7	G8
M (mg)	51	51	51	51	51	51	51	51
HPMCE15 (mg)	75	100	125	150	75	100	125	150
PEG 400 (mg)	2.5	2.5	2.5	2.5	5	5	5	5

DW mL	10	10	10	10	10	10	10	10

Quantities of PEG-400 are expressed in terms of %w/w of polymer (HPMCE15)

Table 1C: Composition of different formulations containing HPMCE15 plasticized with glycerol

Components	Formulation							
	H1	H2	H3	H4	H5	H6	H7	H8
M (mg)	51	51	51	51	51	51	51	51
HPMCE15 (mg)	75	100	125	150	75	100	125	150
GLY (mg)	2.5	2.5	2.5	2.5	5	5	5	5
DW (ml)	10	10	10	10	10	10	10	10

Quantities of GLY are expressed in terms of %w/w of polymer (HPMCE15)

Evaluation of M containing films

Film Thickness

The thickness of film was measured using Digimatic caliper, Mitutoyo, (ABSOLUTE). The thickness of each film was determined at ten different positions. The determination was performed in triplicate and the average was calculated. The standard deviation of thickness was computed from the mean value.

Drug Content

A sample of 6cm^2 was dissolved in 10 ml methanol and shake for 2 minutes to extract drug from formulation and filtered through whatman filter paper and analyzed spectrophotometrically at 341 nm using methanol as blank. The mean and standard deviation of drug content of three randomly selected films were calculated.

Folding Endurance

The folding endurance of the films was determined by repeatedly folding one film at the same place till it broke or folded up to 300 times, which is considered satisfactory to reveal good film properties. The number of times film could be folded at the same place without breaking gave the value of the folding endurance.

Percent Moisture Uptake

Percentage moisture uptake was determined by keeping the films (2 x 3 cm^2) in an environment chamber of 40^{0}C temperature and 75% RH. After 1 week, the films were taken out, weighed and the percentage moisture uptake was calculated using the following formula and performed in triplicate.

$$\text{Percentage Moisture Uptake} = \frac{(\text{Final Weight} - \text{Initial Weight})}{(\text{Final Weight})} \times 100$$

Weight of film

Films (size of 2 × 3 cm^2) were cut from different areas of film. The weight of each film was taken and the weight variation of six films was calculated. The standard deviation of weight was computed from the mean value.

Mechanical properties

Mechanical properties of films were evaluated using a Brookfield, USA texture analyzer equipment equipped with a 5Kg load cell. Films are held between two clamps positioned between 3cm. During measurement the films were pulled at rate of 2mm/sec. The force and elongation were measured when film breaks. Three mechanical properties namely tensile strength, elastic modulus and % elongation were calculated.

Tensile strength

Tensile strength is calculated by formula

$$\text{Tensile strength} = \frac{\text{Load at failure} \times 100}{\text{Film thicknes} \times \text{film width}}$$

Percentage Elongation

It is calculated as

$$\% \text{ Elongation} = \frac{\text{Increase in length}}{\text{Original length}} \times 100$$

Surface pH study

A combined pH electrode is used for this purpose. Fast dissolving film was slightly wetted with distilled water. The pH was measured by bringing the electrode in contact with the surface of the film and performed in triplicate.

In vitro disintegration test

Disintegration test was performed according to the specifications of oral dispersible tablet reported in European Pharmacopoeia by using samples of area 6 cm^2. The disintegration time is the time when a film starts to break or disintegrate. It was determined visually in a petridish containing 25 ml water, and performed in triplicate.

In vitro dissolution test

The dissolution test was performed according to USP type I Basket apparatus (Electrolab Dissolution tester, EDT-08Lx). The dissolution medium was 900 ml freshly prepared pH 6.8 phosphate buffer, maintained at 37 ± 1^0C and stirred at 100 rpm. Montelukast concentrations were assayed spectrophotometrically at 341 nm. The results were expressed in average of three determinations.

Stability study of films

Accelerated stability studies were performed at 40 ^{0}C/75% RH as per the ICH guidelines. Various parameters such as drug content and in vitro release were determined during study. There was no color change observed after stability study. The in vitro drug release profile of film containing PEO shown in (Table 6). No major difference was found between evaluated parameters before and after storage and all are in acceptable limits.

RESULTS AND DISCUSSION

The present study comprises the use of Montelukast sodium fast dissolving film prepared by solvent casting method. The PEO and HPMCE15 were used as film formers and glycerol and PEG-400 as plasticizer. The prepared films were tested for thickness, surface pH, drug content, percent moisture uptake, tensile strength, percent elongation, weight variation, folding endurance, disintegration time, stability study (Table 3,4,5,6) and dissolution study (Fig. 3) . The use of PEO instead of HPMCE15 as film former showed better results desired for fast dissolving films.

All formulations made by solvent casting method. Formulations of PEO as film former plasticized with only glycerol in different concentrations (Table 1A, 1B and 1C). PEO plasticized with PEG-400 does not form films. HPMCE15 films are also plasticized with glycerol as well as PEG-400. OTF containing PEO with glycerol in different concentrations (5%, 10% and 15%) gives better results as compared to films of HPMCE15 with glycerol or PEG-400. Films made up of PEO showed folding endurance more than 250 and HPMCE15 showed only more than 130. Also tensile strength and percent elongation of films of PEO was more than that of films of HPMCE15. In thickness, weight, surface pH does not have any drastic changes when concentrations of glycerol or PEG-400 were changes in all formulations (Table 2, 3). Disintegration is the important factor in OTF's. The disintegration time of films of PEO was less than 6 sec. But disintegration time of films of HPMCE15 was more than 90 sec (Table 5A and Table 5B). Also in drug release PEO films gives more than 90% drug release within 8 min. Films made up of HPMCE15 gives 80% drug release up to 30 min (Fig.3).Stability study of films of PEO with 5% glycerol was carried out as per ICH guidelines, and the formulation was stable after 90 days at 40^{0}C and 75% relative humidity (Table 6).

Differential Scanning colorimetry (DSC)

The thermogram of montelukast exhibited endothermic peak at 138.68^{0}C while PEO and HPMCE15 exhibited an endothermic peak 59.27^{0}C and 233.33^{0}C respectively (Fig.1). The peak of Montelukast was slightly shifted by 10-12^{0}C in physical mixture with PEO and HPMC E15.

The DSC thermogram of pure drug and polymers as well as physical mixtures shows identical peaks corresponding to pure drug indicated no chemical interaction between drug and polymer.

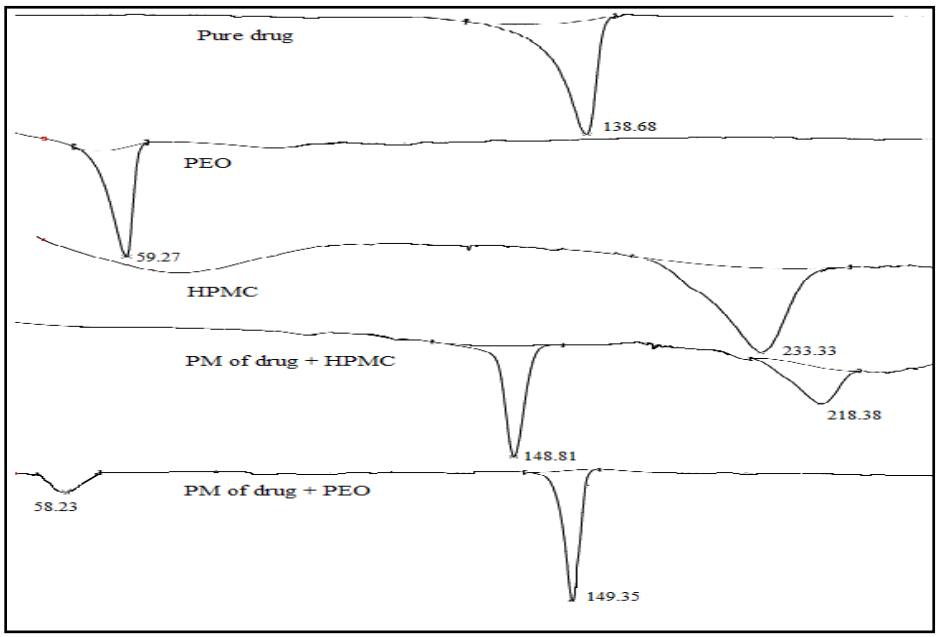

Figure 1: D.S.C. thermograms of drug and its physical mixtures.

Fourier transformed infrared (FTIR) study

The FT-IR studies were carried out for pure drug and along with polymer (Figure.2). Peaks given by drug were present in the FTIR spectra of physical mixture of drug and polymers are nearly equal to each other, it indicates that they were compatible. Thus, shows that there was no interaction between drug and polymer (Table 2).

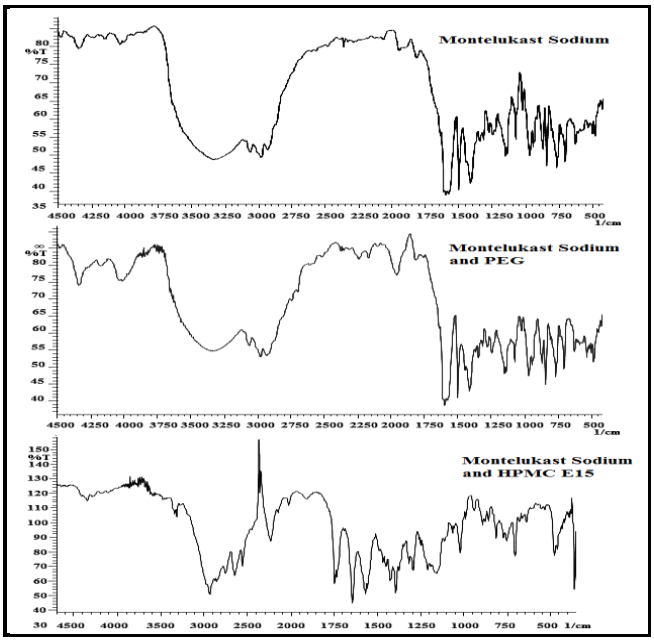

Figure2: F.T.I.R. spectrum of pure drug and its physical mixtures

Table 2:F.T.I.R. interpretation of pure drug and its physical mixtures

Drug peak	Physical mixture with PEO peak	Physical mixture with HPMCE15 peak	Interactions
3396.23, 3062.76, 1587.12, 1490.56, 1143.73, 761.82	3397.06, 3067.17, 1590.12, 1408.4, 1050.26, 768.32	3400.67, 3050.12, 1608.4, 1398.08, 1150.66, 758.22	NO

Evaluation of films

All formulations made by solvent casting method. Formulations of PEO as film former plasticized with only glycerol in different concentrations (Table 3, 4). PEO plasticized with PEG-400 does not form films. HPMCE15 films are also plasticized with glycerol as well as PEG-400. OTF containing PEO with glycerol in different concentrations (5%, 10%, and 15%) gives better results as compared to films of HPMCE15 with glycerol or PEG-400. Films made up of PEO showed folding endurance more than 250 and HPMCE15 showed only more than 130. Also tensile strength and percent elongation of films of PEO was more than that of films of HPMCE15. In thickness, weight, surface pH does not have any drastic changes when concentrations of glycerol or PEG-400 were changes in all formulations.

Table 3: Evaluation of M containing films of PEO

Formul	Thickness (µm)	Folding endurance	% moisture uptake	Drug content (%)	Tensile strength(kg/cm^2)	Percentage elongation (cm %)	Surface pH	Weight of film
F1	32.82 ± 0.23	330.58 ± 1.07	1.84 ± 0.15	94.11 ± 1.01	26.24 ± 0.78	69.95 ± 1.23	6.8 ± 0.45	25.58 ± 1.07
F2	45.72 ± 0.95	300.45 ± 1.24	2.69 ± 0.51	90.02 ± 0.30	35.54 ± 0.56	61.24 ± 1.54	6.9 ± 0.05	29.45 ± 1.24
F3	53.98 ± 0.38	290.51 ± 1.15	2.95 ± 0.21	90.79 ± 1.66	58.62 ± 0.25	58.50 ± 1.56	6.8 ± 0.07	33.51 ± 1.15
F4	63.72 ± 0.88	264.3 ± 1.35	3.03 ± 0.14	86.44 ± 0.39	74.76 ± 0.98	36.71 ± 2.30	6.85 ± 0.08	50.3 ± 1.35
F5	35.04 ± 0.85	340.13 ± 2.31	1.68 ± 0.42	97.15 ± 0.83	32.26 ± 0.76	91.08 ± 3.14	6.99 ± 0.11	30.13 ± 0.31
F6	46.9 ± 0.58	325.36 ± 2.51	0.59 ± 0.02	94.2 ± 1.23	45.34 ± 0.84	79.36 ± 4.09	6.92 ± 0.15	34.36 ± 0.51
F7	55.58 ± 0.81	270.03 ± 2.2	0.24 ± 0.02	89.71 ± 0.67	54.94 ± 0.17	65.84 ± 5.02	6.84 ± 0.06	40.03 ± 0.2
F8	66.12 ± 0.22	250.13 ± 1.31	0.36 ± 0.07	86.44 ± 0.91	68.76 ± 0.66	58.56 ± 2.78	6.78 ± 0.04	45.13 ± 0.31
F9	37.6 ± 0.69	350.4 ± 1.22	0.70 ± 0.53	91.8 ± 0.53	22.26 ± 0.26	144.05 ± 3.61	6.83 ± 0.39	34.4 ± 1.22
F10	51.46 ± 0.83	326.13 ± 2.70	0.70 ± 0.15	92.44 ± 2.27	31.54 ± 0.56	124.08 ± 1.64	6.86 ± 0.12	38.13 ± 0.70
F11	56.8 ± 0.4	304.96 ± 4.77	0.40 ± 0.07	89.59 ± 2.28	42.28 ± 0.97	100.26 ± 3.05	6.76 ± 0.06	43.96 ± 0.77
F12	68.46 ± 0.58	275.43 ± 2.57	0.22 ± 0.02	89.08 ± 1.51	58.36 ± 0.24	84.64 ± 4.22	6.81 ± 0.12	48.43 ± 0.57

Each reading was an average of three determinations. (SD ± n=3)

Table 4: Evaluation of M containing films of HPMC E15

Formula	Thickness (µm)	Folding endurance	% moisture uptake	Drug content (%)	Tensile strength (kg/cm^2)	Percentage elongation (cm %)	Surface pH	Weight of film
G1	145 ± 0.010	165.21 ± 0.77	0.307 ± 0.03	90.8 ± 1.27	120.45 ± 0.23	20.56 ± 1.34	6.69 ± 0.03	65.21 ± 0.77
G2	150 ± 0.015	156.09 ± 0.53	0.210 ± 0.06	86.66 ± 0.66	155.23 ± 0.47	18.34 ± 1.66	6.65 ± 0.06	66.09 ± 0.53
G3	150 ± 0.05	137.05 ± 1.24	0.149 ± 0.02	84.84 ± 0.86	167.87 ± 0.28	16.87 ± 1.72	6.72 ± 0.1	67.05 ± 1.24
G4	165 ± 0.020	128.90 ± 1.56	0.290 ± 0.12	89.12 ± 0.58	181.45 ± 0.32	11.76 ± 2.36	6.76 ± 0.09	68.90 ± 1.56
G5	160 ± 0.015	168.85 ± 0.74	0.580 ± 0.05	91.51 ± 1.54	100.43 ± 0.54	22.68 ± 1.86	6.67 ± 0.06	68.85 ± 0.74
G6	166 ± 0.025	159.54 ± 1.65	0.086 ± 0.07	96.36 ± 0.55	112.76 ± 0.76	19.12 ± 1.61	6.63 ± 0.17	69.54 ± 1.65
G7	170 ± 0.025	140.92 ± 0.97	0.253 ± 0.04	83.03 ± 0.86	124.73 ± 0.32	18.56 ± 1.22	6.75 ± 0.08	70.92 ± 0.97
G8	175 ± 0.015	131.89 ± 0.76	0.709 ± 0.14	88.48 ± 0.72	144.34 ± 0.63	15.34 ± 2.86	6.69 ± 0.06	71.89 ± 0.76
H1	178 ± 0.025	166.85 ± 0.2	0.926 ± 0.04	87.87 ± 0.78	100.23 ± 0.34	22.40 ± 1.53	6.87 ± 0.06	66.85 ± 0.2
H2	184 ± 0.015	157.54 ± 0.23	0.310 ± 0.02	91.51 ± 1.12	112.54 ± 0.56	21.24 ± 1.76	6.83 ± 0.08	67.54 ± 0.23

H3	192 ± 0.005	147.92 ± 0.42	0.427 ± 0.06	89.69 ± 1.32	118.67 ± 0.98	18.36 ± 1.38	6.92 ± 0.16	67.92 ± 0.42
H4	190 ± 0.010	138.62 ± 0.76	0.233 ± 0.17	90.30 ± 0.76	126.23 ± 0.23	16.65 ± 2.69	6.86 ± 0.08	68.62 ± 0.76
H5	180 ± 0.025	167.45 ± 0.46	0.600 ± 0.05	92.12 ± 0.46	80.32 ± 0.46	25.26 ± 1.24	6.75 ± 0.1	67.45 ± 0.46
H6	185 ± 0.035	148.24 ± 0.85	1.025 ± 0.07	86.66 ± 1.34	87.54 ± 0.77	23.86 ± 2.42	6.67 ± 0.09	68.24 ± 0.85
H7	187 ± 0.010	139.75 ± 1.14	0.186 ± 0.07	84.24 ± 0.62	90.87 ± 0.56	21.34 ± 1.72	6.78 ± 0.17	69.75 ± 1.14
H8	194 ± 0.035	130.15 ± 0.63	0.924 ± 0.03	92.72 ± 0.81	97.46 ± 0.24	19.05 ± 1.86	6.72 ± 0.04	69.15 ± 0.63

Each reading was an average of three determinations. (SD ± n=3)

Table 5A: In-vitro disintegration test of M containing films of PEO

Formulation	Disintegration Time in Sec	Formulation	Disintegration Time in Sec	Formulation	Disintegration Time in Sec
F1	4.33 ± 0.57	F5	4.33 ± 0.57	F9	6 ± 1
F2	6 ± 0	F6	5.33 ± 0.57	F10	7.33 ± 0.57
F3	6.33 ± 0.57	F7	4.33 ± 0.57	F11	8.66 ± 0.58
F4	7 ± 1	F8	5.66 ± 1.52	F12	8.33 ± 1.15

Each reading was an average of three determinations. (SD ± n=3)

Table 5B: In-vitro disintegration test of M containing films of HPMCE15

Formulation	Disintegration Time in Sec	Formulation	Disintegration Time in Sec	Formulation	Disintegration Time in Sec
G1	120 ± 2	G7	131.6 ± 3.51	H4	102.3 ± 2.08
G2	116.3 ± 7.09	G8	135 ± 3.51	H5	91 ± 1
G3	124.6 ± 2.51	H1	94.6 ± 3.51	H6	96.6 ± 1.52
G4	130.6 ± 3.05	H2	90.3 ± 0.57	H7	99.6 ± 2.51
G5	115 ± 3	H3	98.6 ± 0.57	H8	102 ± 3.78
G6	128.6 ± 1.15				

Each reading was an average of three determinations. (SD ± n=3)

In vitro disintegration time

Disintegration is the important factor in OTF's. It was observed that films of PEO disintegrate immediately as compared to films of HPMCE15. The disintegration time of films of PEO was less than 6 sec. But disintegration time of films of HPMCE15 was more than 90 sec (Table 5).

In-vitro dissolution studies

In vitro dissolution study of montelukast sodium fast dissolving films was carried out in pH 6.8 phosphate buffer solution (Figure.3). Drug release PEO films gives more than 90% drug release within 8 min. Films made up of HPMCE15 gives 80% drug release up to 30 min

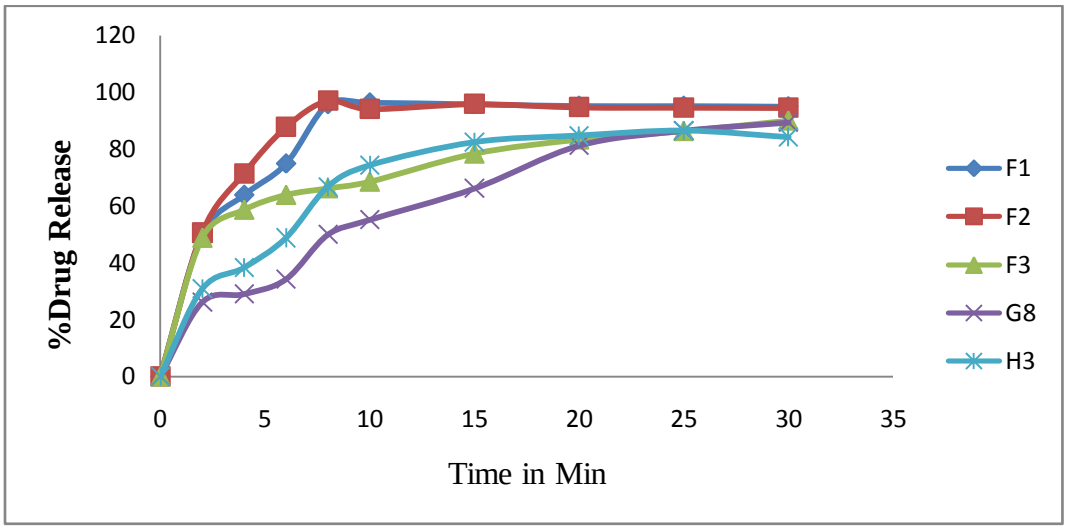

Figure 3: Release profile of Montelukast sodium from fast dissolving films

Stability studies

Stability study of films of PEO with 5% glycerol was carried out as per ICH guidelines, and the formulation was stable after 90 days at 40^0C and 75% relative humidity (Table 6). There was no any drastic effect observed on drug content and drug release.

Table 6: Stability studies

Evaluation parameters	Before stability Storage	After 15days storage	After 45 days storage	After 90 days Storage
Drug content (%)	90%	89%	88%	86%
Percent drug release in 6.8 pH phosphate buffer after 20 min.	92.441%	91.667%	91.569%	88.849%

CONCLUSION

The present study reveals the use of fast dissolving film prepared by solvent casting technique using Montelukast sodium as a model drug. The technique used was found advantageous compared to other method especially when cost, equipment requirements and processing comfort

is concerned. The prepared Montelukast loaded OTF can be used in emergency condition of severe asthmatic attacks. It could find a better application for patient compliance and occurrence especially in children. The comparison study by using PEO and HPMCE15 as film forming polymer was performed. The results obtained for film disintegration and dissolution time tested orally correlated well with those obtained by the visual method. There was considerable reduction in film strength and increase in percent elongation of film with increase in glycerol content. The result showed that film containing PEO with 5% glycerol showed better disintegration, dissolution and folding endurance when compared with film containing HPMCE15. Hence, the film containing PEO was used for further optimization where the optimized batch depicted disintegration time of less than 6 sec, complete drug release within 8 min, percent elongation as 61.24 cm % and folding endurance more than 250 .

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REFERENCE

1. Basani G, Subash VK, Guru S, Madhusudhan YR. Overview on fast dissolving films. Int J Pharma Pharm Sci 2010; 2(3): 29-33.
2. T Jong GW, Van Der Linden PD, Bakker EM, Van Der LN, Elamd IA, Stricker BH, Van Den Anker JN. Unlicensed and off-label drug use in a paediatric ward of a general hospital in the Netherlands. Eur J Clin Pharmaco 2002; l58: 293-297.
3. Jurgen D. Quest of Tomorrow's Medicine friability, Springer-Verlag New York. Drug Dev Ind Pharm 1999; 28(6): 711-715.
4. http://pediatrics.aappublications.org/content/100/1/143.full.pdf+html
5. Dali S, Subhashis C, Sanjay S, Brahmeshwar M. Mouth Dissolving Tablets I: An Overview of Formulation Technology. Sci Pharm 2009; 77: 309–326.
6. Pravin VS, Dumbare AS, Gadhave MV, Jadhav SL, Sonawane AA, Gaikwad DD. Formulation and evaluation of rapidly disintegrating film of amlodipine besylate. J Drug Deliv Ther 2012; 2(2): 72-75.
7. Dixit RP, Puthli SP. Oral strip technology: Overview and future potential. J Contr Rel 2009; 92(6): 94-107.

8. Gupta A, Mishra AK, Gupta V, Bansal P, Singh R, Singh A. Recent Trends of Fast Dissolving Tablet –An Overview of Formulation Technology. Int J Pharm Bio Arch 2010; 1(1): 1 – 10.
9. http://www.toxicology.org/pr/ToxTopics/TT1_Asthma.pdf
10. http://www.cdc.gov/asthma/impacts_nation/AsthmaFactSheet.pdf
11. Xaber B, Prudence B, Henning V. Bronchial asthma and COPD due to irritants in the workplace – an evidence-based approach. J Occup Med Toxicol 2012; 7(19): 1-31.
12. http://www.thoracic.org/statements/resources/eoh/burden1-11.pdf
13. Vijaykumar G, Ajaykumar P, Satishkumar P, Karunasri S, Raghavender K, Priya P. Development and evaluation of fast dissolving film of montelukast sodium. World J Med Pharm Bio Sci 2011; 1(1): 06-12.
14. Valerei HN, Judith A, Greta S. Montelukast sodium polymorphs, United State Patent US 2005/0187244 A1,25 August 2005.
15. Hiroyoshi S, Kazumi T, Misao N, Katsuhiko M, Tadao T, Hirotaka Y, Naoki I, Kazuyuki H, Mayumi Y, Yasutomi K, Yoshinori I. Preparation of a fast dissolving oral thin film containing dexamethasone: A possible application to antiemesis during cancer chemotherapy. Eur J Pharm Biopharm 2009; 73: 361–365.
16. Rakeshkumar B, Nirika B, Pradipkumar K. Advances in Formulation of Orally Disintegrating Dosage Forms: A Review Article. Indo Glo J Pharm Sci 2011; 1(4): 328-353.
17. Raymond RC, Paul SJ, Quinn ME. Handbook of Pharmaceutical Excipients. American Pharmaceutical Association. Washington, 2009.
18. Ming JC, Gloria T, Charles B, Caroline C, Gavin W, Ivonne S. Castable edible pharmaceutical films. Annual Meeting and Exposition of the American Pharmaceutical Scientists, November 11-15, 2007: 1-7.
19. Ming JC, Gloria T, Charles B, Caroline C, Gavin W, Ivonne S. Film forming polymers in oral films. Annual Meeting and Exposition of the American Pharmaceutical Scientists, October November 29-2, 2006: 1-5.