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Fast Dissolving Films of Chlorphneiramine Maleate

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ABSTRACT

For more patient compliance there is a great demand for novel dosage form. Fast dissolving drug delivery system offers a solution for the patients who prefer oral route of drug administration without difficulty in swallowing. Fast dissolving films offers the simplest route of administration which is not painful and which do not require water for swallowing. Chlorpheniramine maleate is the First Generation alkyl amine antihistamine and used to relieve symptoms of allergy, hay fever, and common cold. These symptoms include rashes, watery eyes, itchy eyes/nose/throat/skin, cough, runny nose, and sneezing. In present study the aim was to formulate and evaluate fast dissolving films of Chlorpheniramine maleate. The films was prepared by solvent casting method, the superdisintegrants Crospovidone (2,4,6,8,10% w/w) and Microcrystalline Cellulose (5,10,15,20,25% w/w) were used in different concentrations with HPMC & PVA as a film forming base. Along with polymers and superdisintegrants the plasticizer PEG, mint flavor and sucrose were used in preparation of films. The formulated films were evaluated for thickness measurement, weight variation, folding endurance, disintegration time, *in vitro* drug release. It was concluded that the films containing Crosspovidone shows better drug release and less disintegration time as compared to the films containing Microcrystalline Cellulose.

Keywords: Fast dissolving films, Chlorpheniramine maleate, Compliance, superdisintegrants

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INTRODUCTION

Oral route is the simplest and non- painful route of administration. Oral route is preferred because of its various advantages which includes ease of administration, avoidance of pain versatility and the most important patient compliance. The introduction of fast dissolving films increases the patient compliance especially for the pediatric and geriatric population. Generally geriatric, pediatric and bedridden patient experience difficulties in swallowing the conventional oral dosage form[1]. This difficulty of tablets and capsules are overcome by fast dissolving films. Fast dissolving film is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates and dissolves to release the medication for oromucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed [2]. The development of a fast-dissolving film also provides an opportunity for a line extension in the market place; a wide range of drugs (e.g., neuroleptics, cardiovascular drugs, analgesics, antihistamines, antiasthmatic and drugs for erectile dysfunction) can be considered candidates for this dosage form.[3]

Characteristics required for fast dissolving films [4,5]

- Require no water for oral administration, yet dissolve/disperse/disintegrate in mouth in matter of seconds
- Have a pleasing mouth feel, to increase the patient compliance.
- Have an acceptable taste masking property.
- Subsequent to oral administration, it should leave least or no residue in mouth, this avoids the need of water.
- It should be compatible with the other ingredients, so that films can manufacture easily.

Advantages of Fast Dissolving Films [6, 7]

- The oral or buccal mucosa is highly vascularized; hence drugs can be absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism. And due to which action of drug (e.g Chlorpheniramine maleate) can be seen quickly.
- No risk of choking and obstruction, which increases patient compliance.
- Fast releasing and disintegration within minutes in the mouth.
- Reduction in first pass metabolism may lead to reduction in the dose.
- Improved oral bioavailability of drugs
- Available in different size and shape, which increases the elegance of films

Disadvantages of Fast Dissolving Films [8]

- Drugs which are not stable at buccal pH cannot be administered
- Drug in large dose cannot be administered.
- It takes Special packaging due to fragile in nature and must be protected from water.
- Drugs which are irritate to the mucosa which cannot be administered by this route.

MATERIALS AND METHODS

Chlorpheniramine maleate was obtained as gift sample from Unichem, Baddi, Crospovidone, Microcrystalline cellulose, HPMC & PVA were purchased from SD fine chem. Other excipients used were analytical grade. Fast Dissolving Films can be prepared by any of the following methods [9]

1. Solvent casting
2. Semisolid casting
3. Hot melt extrusion
4. Solid dispersion extrusion
5. Rolling methods

The fast dissolving films of Chlorpheniramine maleate was prepared by Solvent Casting Method

The formulations were prepared as per Table no.1. The polymers PVA and HPMC was weighed accurately and dissolved in distilled water. Then drug and other ingredients are added with continuous stirring with a magnetic stirrer. At last the plasticizer (PEG) was added with constant stirring. The resultant homogenous solution were poured in Petridish. Then the films were dried in an oven at 50ºC for 24 h.

Table-1: Formulation of fast dissolving films of Chlorpheniramine maleate

Code	Drug (mg)	HPMC (%w/v)	PVA (%w/v)	Crospo-vidone (%w/w of polymer)	MCC (%w/w of polymer)	PEG (%w/w of polymer)	Citric acid (%w/w of polymer)	Sucrose (%w/w of polymer)	Menthol (%w/w of polymer)
F1	30		3.0	2.0	-	30	4.0	4.0	8.0
F2	30		3.0	4.0	-	30	4.0	4.0	8.0
F3	30		3.0	6.0	-	30	4.0	4.0	8.0
F4	30		3.0	8.0	-	30	4.0	4.0	8.0
F5	30		3.0	10	-	30	4.0	4.0	8.0
F6	30		3.0	-	5	30	4.0	4.0	8.0
F7	30		3.0	-	10	30	4.0	4.0	8.0
F8	30		3.0	-	15	30	4.0	4.0	8.0
F9	30		3.0	-	20	30	4.0	4.0	8.0

F10	30		3.0	-	25	30	4.0	4.0	8.0
F11	30	4.0		2.0	-	30	4.0	4.0	8.0
F12	30	4.0		4.0	-	30	4.0	4.0	8.0
F13	30	4.0		6.0	-	30	4.0	4.0	8.0
F14	30	4.0		8.0	-	30	4.0	4.0	8.0
F15	30	4.0		10	-	30	4.0	4.0	8.0
F16	30	4.0		-	5	30	4.0	4.0	8.0
F17	30	4.0		-	10	30	4.0	4.0	8.0
F18	30	4.0		-	15	30	4.0	4.0	8.0
F19	30	4.0		-	20	30	4.0	4.0	8.0
F20	30	4.0		-	25	30	4.0	4.0	8.0

Compatibility Studies by FTIR

Compatibility studies were performed using FT-IR Spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and polymer were studied by making a KBr disc. The characteristic absorption peaks of CPM were obtained at different wave numbers in different samples. The peak obtained in the spectra of each formulation correlates with the peaks of drug spectrum. This indicates that the drug is compatible with the formulation components. The spectra for all formulations are shown below in Figure 1,2,&3.

Evaluation of Fast Dissolving Films

Physical appearance and surface texture of films[10]

This parameter was checked simply with visual inspection of films and evaluation of texture by feel or touch.

Weight uniformity of films [11]

The films of size 2.5×2.5 cm were weighed individually using digital weighing balance and the average weight calculated.

Thickness of films[11]

Thickness of films was measured by using Screw Guage with least count of 0.01mm at different spots of films. The thickness was measured at three different spots of the films and average was taken.

Folding Endurance

Folding endurance measures the flexibility of films. Folding endurance of films was measured repeatedly folding a small strip of films at the same place till it broke. The number of times films could be folded at the same place, without breaking gives the value of folding endurance.

Surface pH of films[11]

For determination of surface pH of films, the films were allowed in contact with 1ml of distilled water. The surface pH was noted by bringing a combined glass electrode near the surface of films

and allowing equilibrate for 1 minute.

***In Vitro* disintegration time of films [10]**

Disintegration test was performed in disintegrating time testing apparatus. Water used as medium. The films were placed in the tubes of the DT apparatus and disintegration time was recorded.

***In-vitro* Dissolution Studies [12]**

In Vitro dissolution of Chlorpheniramine maleate fast dissolving film was studied in Type 1 (rotating paddle) dissolution test apparatus, 900ml phosphate buffer pH 6.8 was used as medium. The stirrer was adjusted to rotate at 50 rpm. The temperature of dissolution medium was maintained at 37±0.5^{0}C throughout the experiment. One film was used in each test. Samples of dissolution medium (5ml) were withdrawn by means of pipett, at known intervals of time and analyzed for drug release by measuring the absorbance at 261nm. The volume withdrawn at each interval was replaced with fresh quantity of dissolution medium.

RESULTS AND DISCUSSION

Table 2: Evaluation of Fast Dissolving Films of Chlorpheniramine Maleate

Formulation Code	Average Weight (mg) ± SD, n=3	Average Thickness (mm) ± SD, n=3	Average Disintegration Time (sec) ±SD, n=3	Average Surface pH ±SD, n=3	Folding Endurance ± SD, n=3
F1	51.08±0.12	0.130±0.015	11±0.342	6.27±0.153	260±1.732
F2	53.21±0.24	0.140±0.005	09±0.165	6.41±0.100	263±1.000
F3	54.19±0.08	0.140±0.020	08±0.112	6.62±0.115	271±2.645
F4	57.14±0.24	0.145±0.010	10±0.171	6.70±0.152	265±2.000
F5	58.05±0.09	0.150±0.015	11±0.485	6.91±0.152	277±3.000
F6	52.23±0.42	0.140±0.010	14±0.591	6.36±0.057	274±1.453
F7	55.73±0.13	0.145±0.010	13±0.151	6.43±0.152	270±1.674
F8	57.01±0.34	0.145±0.020	12±0.479	6.68±0.100	270±1.375
F9	57.23±0.07	0.150±0.005	15±0.100	6.82±0.057	281±3.310
F10	58.89±0.32	0.150±0.015	15±0.151	7.00±0.173	276±3.460
F11	64.16±0.12	0.145±0.005	10±0.057	6.14±0.157	280±1.492
F12	64.29±0.35	0.150±0.020	12±0.076	6.42±0.100	276±2.104
F13	66.87±0.06	0.155±0.005	11±0.115	6.58±0.173	282±1.372
F14	67.89±0.46	0.155±0.010	14±0.152	6.75±0.182	281±3.141
F15	69.72±0.32	0.155±0.020	13±0.056	6.86±0.136	279±3.462
F16	65.74±0.52	0.160±0.010	18±0.105	6.23±0.152	281±1.743
F17	66.04±0.16	0.165±0.010	19±0.025	6.38±0.321	280±2.245
F18	67.67±0.35	0.165±0.005	14±0.110	6.55±0.057	282±2.743
F19	68.92±0.64	0.170±0.010	21±0.102	6.84±0.037	281±1.985
F20	69.98±0.14	0.175±0.015	20±0.104	6.93±0.162	285±3.376

Physical appearance and surface texture of films were found to have smooth surface and they are

elegant enough to see. The physicochemical evaluation data presented in Table 2 indicating thickness of the films varies from0.130 to 0.175mm, In all the cases the calculated standard deviation values are very low which suggest that the prepared films were uniform in weight. The weight of films varies from 51.08 to 69.98 mg.In all the cases the calculated standard deviation values are very low which suggest that the prepared films were uniform in thickness. The folding endurance of the films varies from 260 to 285.Since the Surface pH of films was found to be around neutral pH, there will not be any kind irritation to the mucosal lining of the oral cavity. All the formulations of fast dissolving films were found to disintegrate in less than 30 sec. In vitro disintegration time was found to decrease with increase in concentration of superdisintegrants used in formulations. further increase in the concentration of crospovidone and MCC, increased the disintegration time due to blockade of capillary pores which prevents the entry of fluid in to the film.

Table 3: *In-Vitro* dissolution of fast dissolving films of CPM (F1-F10)

Time (min)	Percent Cumulative Drug Release									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
5	65.72	68.32	69.89	68.83	68.21	59.34	61.76	67.67	66.94	66.21
10	67.89	72.19	73.78	72.89	71.78	65.78	69.78	71.89	71.13	70.17
15	75.24	79.77	81.32	79.87	79.02	73.89	75.45	77.94	76.87	75.42
20	80.87	82.32	85.57	83.76	82.41	80.12	81.54	84.65	82.98	81.76
25	86.42	88.54	92.21	89.21	88.76	84.67	85.62	91.23	90.76	88.87
30	94.98	95.87	99.14	98.22	97.92	91.88	93.34	98.45	96.27	94.54

Table 4: *In-Vitro* dissolution of fast dissolving films of CPM (F11-F20)

Time (min)	Percent Cumulative Drug Release									
	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20
5	58.42	61.76	70.11	63.17	62.41	56.23	62.21	68.42	65.86	62.13
10	63.78	65.12	73.78	68.53	66.25	65.97	66.97	70.31	69.74	67.53
15	67.78	69.23	77.46	71.89	70.92	69.76	71.43	75.12	73.84	72.42
20	73.77	75.21	81.23	77.79	76.58	77.12	76.73	81.56	78.72	79.71
25	78.56	81.34	87.71	82.45	81.62	80.72	82.65	88.76	84.49	83.72
30	83.67	87.78	97.86	92.23	89.29	85.23	87.43	95.23	92.84	89.78

It was found that formulation containing 6% Crospovidone with PVA shows 99.14% &97.86% drug release in 30 minutes. and formulations containing 15% microcrystalline Cellulose with PVA shows 98.45% & 95.23% drug release in 3o minutes. And formulation containing 6% Crospovidone with HPMC shows 97.86% drug release and formulations containing 15% Microcrystalline Cellulose with HPMC shows 95.23% drug release. This shows the effectiveness of Crospovidone over Microcrystalline Cellulose.

CONCLUSION

The present study was undertaken for formulation and development of fast dissolving films of Chlorpheniramine maleate. The FTIR shows that that the drug is compatible with the formulation components. The films were uniform in weight and thickness. The films shows minimum disintegration time and % drug release with Crospovidone. CPM is an Anti-histaminic drug and used to relieve symptoms of allergy, hay fever, and common cold. To get instant relive from such allergies fast dissolving films of CPM can formulate.

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