Research Article

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Formulation, and evaluation of Fast Dissolving Oral Films of Diphenhydramine Hydrochloride

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ABSTRACT

The objective of present study was to develop matrix type oral disintegrating film therapeutic systems of Diphenhydramine Hydrochloride using various polymers such as HPMC, Ethyl cellulose polymers as matrix formers by Solvent casting method. Results revealed that prepared films showed good physical characteristics, no drug-polymer interaction and no skin irritation was observed. The in vitro release study revealed that F5 formulation showed maximum release in 240 sec. For F5 Formulation In-vitro disintegration time was found to be 30sec, Thickness was 0.25mm, Folding endurance 79 and Swelling Index was 15.25. The F5 formulation was found to be stable as there was no drastic change in the Physico-chemical properties of the films, which was also confirmed by FTIR. Thus, conclusion can be made that stable oral disintegrating film of Diphenhydramine Hydrochloride has been developed. F5 formulation showed highest cumulative percentage drug release of 98.6% obtained during In vitro drug release studies after 240 sec. Based upon the in vitro dissolution data the F5 formulation was concluded as optimized formulation.

Keywords: Diphenhydramine Hydrochloride, HPMC, Ethyl cellulose, FTIR studies, solvent casting technique, In-vitro drug release studies.

INTRODUCTION

Oral route is most preferred route by medical practitioners and manufacturer due to highest acceptability of patients which favours ease of ingestion, pain avoidance, versatility and more importantly patient compliance[1]. Also, solid oral delivery systems do not require sterile conditions and therefore less expensive to manufacture. About 60% of all dosage forms available are the oral solid dosage form[2].The lower bioavailability, long onset time and dysphasia patients turned the manufacturers to the parenteral and liquid orals.[3] But the liquid orals (syrup, suspension, emulsion etc) have the problem of accurate dosing mainly and parenteral are painful drug delivery systems which leads to patient incompliance.[4] Fast dissolving oral films are most advanced form of solid dosage form due to more flexibility and comfort. It improves the efficacy of API dissolving within minute in oral cavity after the contact with less saliva as compared to fast dissolving tablet[5], without chewing and no need of water for administration. Diphenhydramine Hydrochloride is an antihistamine used to relieve symptoms of allergy, hay fever, and the common cold[6].These

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symptoms include rash, itching, watery eyes, itchy eyes/nose/throat, cough, runny nose, and sneezing. It is also used to prevent and treat nausea, vomiting and dizziness caused by motion sickness[7].

MATERIALS AND METHODS

Materials

Diphenhydramine hydrochloride was collected as a gift sample from Hetero labs, HYD, and various polymers like HPMC, Ethyl cellulose, Sodium Alginate and other excipients were purchased from AR chemicals, Hyderabad.

Methodology

Compatibility studies of drug and polymers[8]

In the formulation of Diphenhydramine Hydrochloride film formation , API and Excipient may interact as they are in close communication with each other, which could lead to the instability of drug. FT-IR spectroscopy was employed to ascertain the compatibility Diphenhydramine Hydrochloride and the selected polymers. The pure drug and drug with excipients were scanned separately.

Formulation design:

Table 1: Formulation Design of Diphenhydramine hydrochloride Oral film

F.Code	Drug	HPMC	Ethyl Cellulose	Sodium Alginate	PEG	DMSO	Crospovidone	Mannitol	Methanol	Distilled water
F1	10	50	-	-	1ml	0.1ml	5mg	5mg	5ml	5ml
F2	10	100	-	-	1ml	0.1ml	5mg	5mg	5ml	5ml
F3	10	-	50	-	1ml	0.1ml	5mg	5mg	5ml	5ml
F4	10	-	100	-	1ml	0.1ml	5mg	5mg	5ml	5ml
F5	10	-	-	50	1ml	0.1ml	5mg	5mg	5ml	5ml
F6	10	-	-	100	1ml	0.1ml	5mg	5mg	5ml	5ml

Preparation method

Solvent casting method[9]

Diphenhydramine Hydrochloride Oral films were formulated by the solvent casting evaporation technique. The drug Diphenhydramine Hydrochloride was diffuse in methanol. Polymers HPMC K15, ethylcellulose and Sodium Alginate were taken in a boiling tube, to this add Diphenhydramine Hydrochloride drug which was previously dissolved in methanol. Sufficient care was taken to prevent the creation of lumps. PEG was taken as a plasticizer and Dimethylsulfoxide as permeation enhancer and added to the mixture and mixed well. It was set aside for 2 hours to exclude any entrapped air and was then transferred into a previously cleaned petri plate (40cm2), drying of films was carried out in vacuum oven at room temperature. Dried films were packed in aluminium foil and stored in a desiccator for further evaluation.

Physico- chemical evaluation[10,11,12]

Physical appearance

All the formulated Diphenhydramine Hydrochloride films were observed for colour, clarity, flexibility, and smoothness.

Thickness of the film

The thickness of each film was measured by using screw gauze. Oral films thickness was estimated at various sites on each patch and the average thickness of the Oral patch was capture as the thickness of the patch.

Weight Variation:

The formulated oral films are to be dried at 600C for 6 hours before trial. Identify the area of4.52 cm2 of film is to be cut in different parts of

the patch and weigh in digitalbalance. The average weight and standard deviation values are to be calculated from the individual weights.

Drug content uniformity

A fast-dissolving film (4.52cm²) was transferred into a graduated flask containing 100 ml of distilled water. The flask was shaken for 4 hr in a mechanical shaker. The solution was filtered and after suitable dilutions with distilled water, the absorbance value was measured at 230 nm using the placebo patch (patch without drug) solution as a blank, and the drug content was calculated.

Folding Endurance

The folding endurance is expressed as the number of folds required to break the specimen or to develop visible cracks. This also gives an indication of brittleness of the film. A strip of 2.5 cm ×cm (6.25cm²) was subjected to folding endurance by folding the patch at the same place repeatedly several times until a visible crack was observed, and the values were reported.

Swelling Index

Film swelling studies are conducted using simulated saliva solution. Each sample is weighed and placed in a pre-weighed stainless steel wire mesh. The mesh containing film sample is submerged into 15ml medium in a plastic container. Increase in the weight of the film was determined at present time interval until a constant weight was observed. The degree of swelling index was calculated using parameters,

$\alpha = wt - wo/w$ □
wt = weight of film at time t.
wo = weight of film at time zero.

Moisture absorption studies

The Oral films were weighed exactly and placed in a desiccators containing aluminium chloride to maintain 79.50% RH. After 3 days, the films were taken out and weighed. The percentage of moisture uptake was calculated using the following formula.

$$\text{Perentage moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Moisture loss studies

Three films were weighed separately and kept in a desiccator contains calcium chloride at 370C for 24 hours. Then the last weight was noted when there was no further change in the weight of the patch. The percentage of moisture loss was calculated using the following formula.

$$\text{Percentage moisture loss} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

In vitro release studies[14]:

The dissolution profile of Diphenhydramine Hydrochloride was carried out in a beaker containing 30 ml of the stimulated salivary fluid (pH 6.8) as a dissolution medium , maintained at 37 ± 0.5 0C. The medium was stirred at 100rpm. Aliquots (5ml) of dissolution fluid were withdrawn at 15,30,45,60,90,120,180, 240 sec time interval and the same amount was replaced with the fresh medium. Samples were assayed spectrometrically at 257 nm.

In-Vitro Disintegration studies

In this method, 2ml of water was placed in petri plate with a film on the surface of water; the time taken for disintegration of the film was measured. This test was done in triplicates and the average value was taken as disintegration time.

RESULTS AND DISCUSSION

Drug - excipient compatibility studies

Compatibility studies were performed using IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and polymer were studied. The peaks obtained in the spectra of each formulation correlates with the peaks of drug spectrum. This indicates that the drug was compatible with the formulation components.

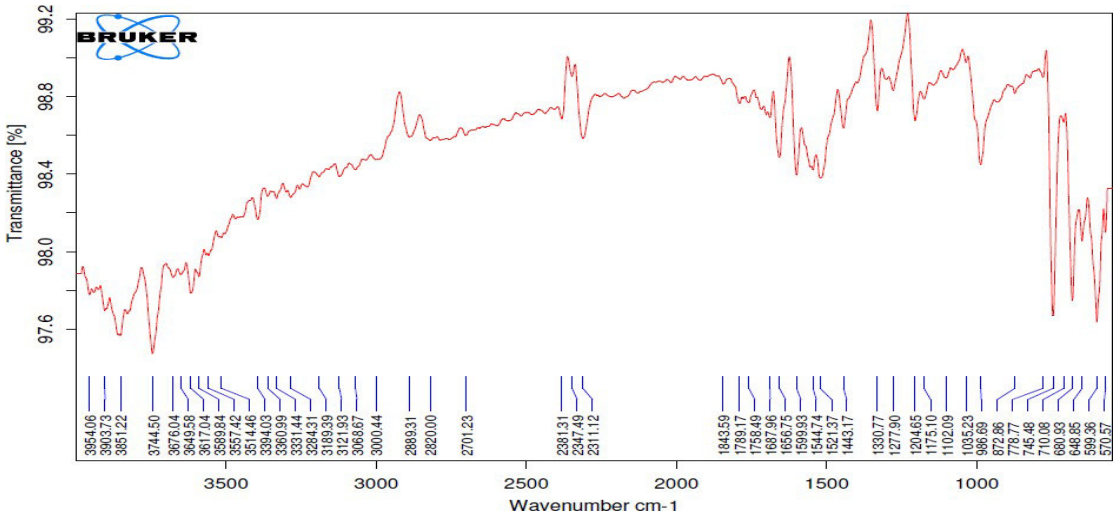

Fig 1: FTIR spectra of pure drug

Physical appearance and surface texture:

These parameters were checked simply with visual inspection of films and by feel or touch. The observation reveals that the films are having smooth surface and they are elegant in appearance.

Thickness of oral films:

The thickness of the films was measured using screw gauge and the average thickness of all films.

Weight Variation of oral films:

The weight of the films was determined using digital balance and the average weight of all films.

Drug content uniformity of oral films:

Diphenhydramine hydrochloride oral films prepared with various polymers were subjected to the valuation for uniform dispersion of drug throughout the patch. In each case films were used and the average drug content was calculated

Folding endurance of oral films

The folding endurance gives the idea of flexible nature of films. The folding endurance was measured manually, films were folded repeatedly till it broke, and it was considered as the end point. The folding endurance was found optimum and the films exhibited good physical and mechanical properties and the average folding endurance of all films.

Swelling index

The swelling index in the oral films ranged from 14.28 to 15.28 %.

% Moisture loss

The moisture content in the oral films ranged from 7.10 to 7.98%. The moisture content in the formulations was found to be increased by increase in the concentration of polymers.

% Moisture absorption

The moisture absorption in the oral films ranged from 8.72 to 9.59%.

Table 2: Physicochemical evaluation data of Diphenhydramine hydrochloride oral films

F.Code	F1	F2	F3	F4	F5	F6
Thickness(mm)	0.31	0.28	0.24	0.25	0.25	0.27
Weight Variation(mg)	47.26	48.12	50.66	46.32	47.12	49.10
Content Uniformity (%)	87.41	89.26	92.84	90.12	96.69	95.28
Folding endurance	74	72	78	76	79	78
Swelling Index	15.07	14.85	14.28	14.16	15.25	15.21
% Moisture loss	8.65	8.75	8.90	8.45	7.23	8.79
% Moisture absorption	10.26	10,52	9.72	9.53	8.76	10.21

In-Vitro Disintegration Studies

Table 3: In vitro disintegration studies of different formulations i.e., F1-F6

S.NO	FORMULATION	DISINTEGRATION TIME (SEC)
1	F1	55
2	F2	57
3	F3	43
4	F4	45
5	F5	30
6	F6	42

In-Vitro Dissolution Studies

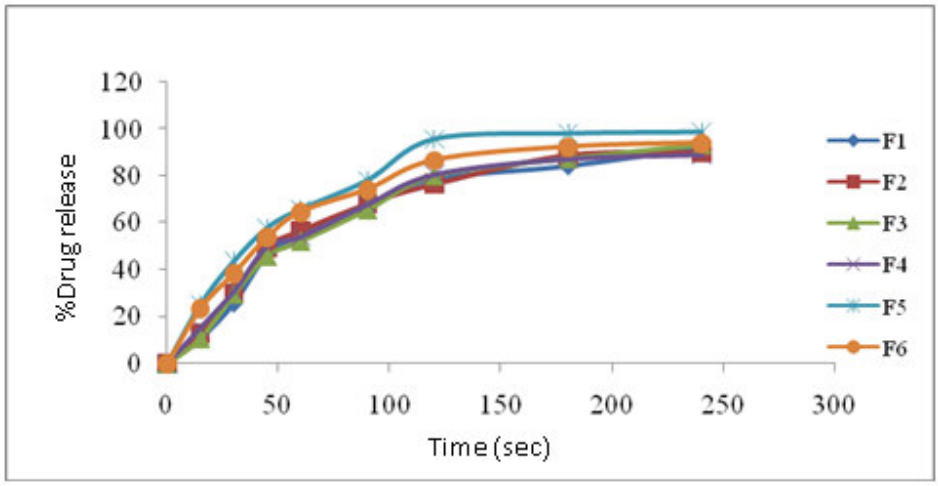

Fig :2 Disintegration studies of different formulations

In-Vitro Dissolution Studies

Table 4:% drug release from the different formulations i.e., F1 F6 of Fast dissolving oral thin films.

S.NO	TIME (sec)	F1(%)	F2 (%)	F3(%)	F4 (%)	F5 (%)	F6 (%)
1	0	0	0	0	0	0	0
2	15	10.81	12.98	10.76	15.43	25.42	23.67
3	30	25.92	30.12	29.67	30.97	43.67	38.86
4	45	46.78	49.67	45.76	50.12	57.87	53.98

5	60	54.78	56.76	52.12	54.13	65.78	64.78
6	90	67.54	68.25	65.54	67.98	78.12	74.35
7	120	78.87	76.59	79.98	80.67	95.6	86.76
8	180	84.43	88.98	87.34	87.34	98.0	92.45
9	240	92.4	90.14	93.12	89.12	98.6	94.12

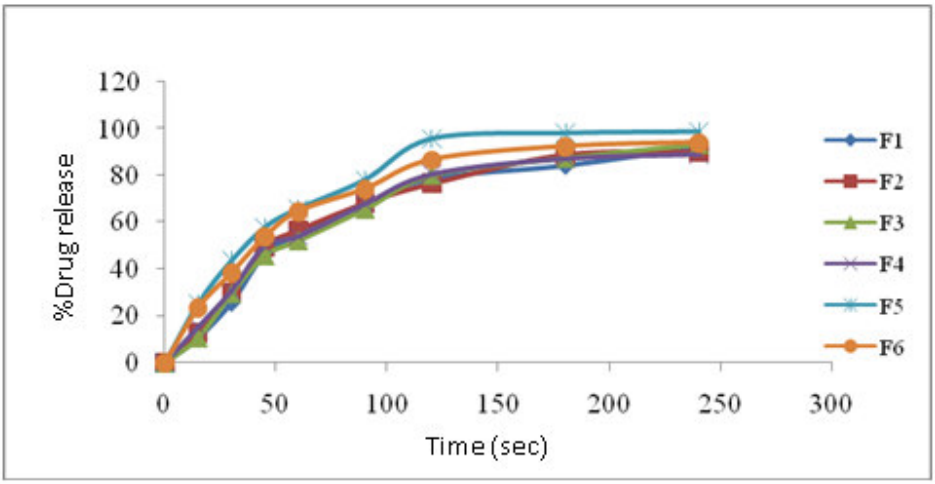

Fig 3 : In vitro drug release of (F1- F6) formulation

SUMMARY AND CONCLUSION

From this study it was concluded that the oral films containing Diphenhydramine Hydrochloride can be successfully prepared by using release rate controlling polymers. Hence these formulations of Diphenhydramine Hydrochloride oral films with having good permeability. In the present study it can be concluded that, FTIR studies revealed that there is no incompatibility or interaction between Diphenhydramine hydrochloride and excipients. Formulated oral films gives satisfactory film characteristics like physical appearance, surface texture, weight uniformity, thickness uniformity, folding endurance, surface pH, percentage swelling index, percentage moisture uptake, drug content uniformity, in-vitro drug release. The low values for standard deviation for average weight, thickness, surface pH, percentage swelling index, percentage moisture uptake, in vitro drug release and drug content indicated uniformity within the batches.F5 formulation fulfills the requirement of good fast dissolving oral films formulation. In vitro dissolution studies, formulation F5 released more than 90% drug in 120 sec and 98.6% of drug in 120 sec and sodium alginate polymer is having the less viscosity i.e. 25-30 poise when compared other polymer so , low viscosity indicates more solubility. For F5 formulation, In-vitro disintegration time was found to be 30sec, Thickness was 0.25mm, Folding endurance 79 and Swelling Index was 15.25.So finally it can be concluded that oral films of Diphenhydramine hydrochloride could provide faster action and enhanced bioavailability of drug. A further clinical investigation has to be conducted to establish the safety and efficacy of the developed formulation.

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