Formulation and Evaluation of Mouth Dissolving Film Containing Cetirizine Hydrochloride

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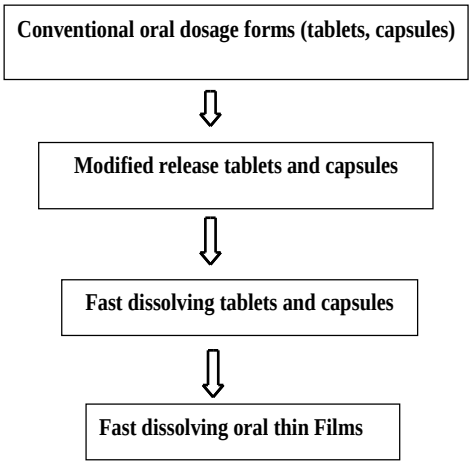
ABSTRACT:
The aim of present research was to develop a fast releasing oral polymeric film, with good mechanical properties, instant disintegration and dissolution, producing an acceptable taste when placed on tongue. Solvent casting method was used to prepare oral films. cetirizine hydrochloride an antihistaminic was incorporated to relieve the symptoms of allergic rhinitis. The polymers selected were HPMC 3cps and PVA. Glycerin was the plasticizer used. Eight batches of films with drug were prepared using different combinations of polymer concentration. The resultant films were evaluated for weight variation, content uniformity, folding endurance, thickness, surface pH, tensile strength, % elongation, % moisture absorption, %moisture loss in vitro disintegration and in vitro dissolution. The optimized films have disintegrated within 28-60sec. The percentage release was varying with concentration of polymer. The films made with HPMC3cps 200 mg released 98.5% of drug in 2min, which was the best release amongst all.
Key word: HPMC 3cps, PVA, oral polymeric Film

I.INTRODUCTION

Oral route is the most preferred route for the delivery of the drugs about 60% of all dosage forms available are till date as it bears various advantages over the other routes of drug administration, but oral drug delivery systems still need some advancements to be made because of their some drawbacks related to particular class of patients which includes geriatric, pediatric and dysphagic patients associated with many medical conditions as they have difficulty in swallowing or chewing solid dosage forms Research and development in the oral drug delivery segment has led to transition of dosage forms from simple conventional tablets or capsules to modified release tablets or capsules to oral disintegrating tablet (ODT) to the recent development of oral fast dissolving films (OFDFs). Orally fast-dissolving film is new drug delivery system for the oral delivery of the drugs. It was developed on the basis of technology of the transdermal patch.

Flow Chart for the Development of Oral Solid Dosage forms



The next generation of dissolvable films is being designed to move beyond immediate-release oral delivery into applications such as implantable, topical, sublingual and gastro-retentive platforms for the delivery of both small and large molecules. This work is the direct result of the flexibility in dissolvable film design and manufacture.

The ideal characteristics of a drug to be selected

- The drug should have pleasant taste.
- The drug to be incorporated should have low dose up to 40 mg.
- The drug should have good stability and solubility in water as well as in saliva.
- It should be partially unionized at the p^H of oral cavity.
- It should have the ability to permeate oral mucosal tissue.

Materials and Methods:

Table: 1 Formulation of HPMC 3cps & PVA films by casting method

SI.no	ingredients	Quantity for 16square inch films			
		F_1	F_2	F_3	F_4
01	HPMC 3cps	500 mg	400 mg	300 mg	200 mg
02	PVA	50 mg	50 mg	50 mg	50 mg
03	Glycerin	300 mg	300 mg	300 mg	300 mg
04	Aspartane	55 mg	55 mg	55 mg	55 mg
05	Cetirizine	40 mg	40 mg	40 mg	40 mg
06	Water	15 ml	15 ml	15 ml	15 ml

Table:2 Formulation of HPMC films by casting method

SI.no	ingredients	Quantity for 16square inch films			
		F_5	F_6	F_7	F_8
01	HPMC 3cps	500 mg	400 mg	300 mg	200 mg
02	Glycerin	300 mg	300 mg	300 mg	300 mg
03	Aspartane	55 mg	55 mg	55 mg	55 mg
04	Cetirizine	40 mg	40 mg	40 mg	40 mg
05	Water	15 ml	15 ml	15 ml	15 ml

II.RESULTS

Table 3: Preformulation studies of API

SI.No.	Characteristics	Results
1.	Organoleptic evaluation	white to off-white crystalline powder, odourless
2.	Solubility analysis	It is freely soluble in water, practically insoluble in solvents like dichloromethane, acetone
3.	Melting point	110-115^o

Drug Excipients Compatibility Study of Physical observation

Compatibility with excipients was confirmed by physical observation. The pure drug and along with its formulation excipients were subjected to compatibility studies & studies were carried out by mixing definite proportions of drug and excipients and kept in glass vials which are stored at 40°C ±2°C &75± 5%RH for one month. Physical observation of sample was done every week for any color change or lump formation; the results of the physical observation are shown in Table:4

Table 4: Results of Compatibility study

S.No	Name of the excipient	Ratio API: Expt	Initial observation	Final observation 40°C/75% RH		Conclusion
				2nd week	4th week	
1	API(Cetirizine hydrochloride)	---	white	white	white	Compatible
2	API+ HPMC3cps	1 :1	white	white	white	Compatible
3	API + Polyvinylalcohol	1 : 1	white	white	white	Compatible

Calibration curve of cetirizine hydrochloride

Development of cetirizine linearity curve by using UV spectrophotometry at λ_{max} 231 nm in distilled water.

Table 5: Calibration curve of Cetirizine

Concentration(µg/ml)	Absorbance (231nm)
0	0
2	0.1393
4	0.2938
6	0.4471
8	0.5849
10	0.7365

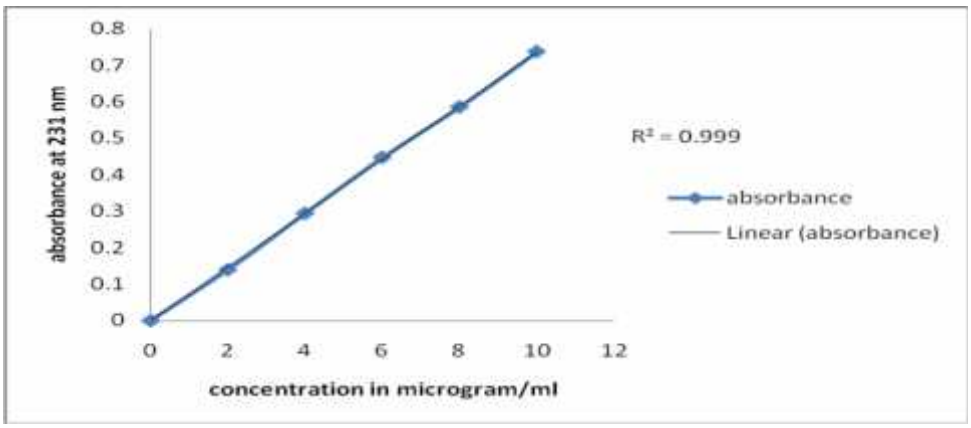


Fig.6 Standard graph of cetirizine hydrochloride

III.EVALUATION OF ORAL THIN FILMS

Eight formulations were prepared using solvent casting method and dried. Films consist of glycerin as a plasticizer and HPMC 3cps and PVA as polymers. Drug loaded films were flexible and transparent. Elegant appearance, good physical properties. Thus these formulations can maintain a smooth and uniform surface when placed on tongue. The prepared films evaluated for

a) Mechanical properties
- Percentage moisture absorption (PMA)
- Percentage moisture loss (PML)
- Tensile strength
- % elongation
- Weight variation
- Thickness
- Surface pH of films

b) Drug content
c) Drug content uniformity
d) Disintegration time
e) *In vitro* dissolution study

Table: 6 Evaluation for weight variation, Thickness, Folding endurance, Surface pH, % Drug content, Disintegration time of oral thin film formulation of cetirizine

Formulation	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
Weight Variation (mg)	1050± 0.0015	989± 0.0015	968± 0.0026	959± 0.0015	898± 0.2015	889± 0.0005	867± 0.0010	859± 0.0019
Thickness (mm)	0.39± 0.010	0.33± 0.070	0.30±0. 015	0.26± 0.015	0.23± 0.005	0.22± 0.010	0.20± 0.010	0.18± 0.005
Folding endurance	300± 3.51	296± 6.08	292± 2.64	290± 1.00	286± 1.52	273± 3.21	265± 1.52	259± 3.21
Surface pH	6.94± 0.030	6.87± 0.115	6.85± 0.005	6.96± 0.152	6.85± 0.020	6.753± 0.005	6.883± 0.035	6.85± 0.005
% Drug content	93.6± 0.100	94.5± 0.208	95.4± 0.152	95.8± 0.152	96.6± 0.100	97.8± 0.115	98.4± 0.115	99.8± 0.208
Disintegration Time (seconds)	60± 2.00	55± 0.57	48± 1.00	45± 1.52	43± 1.52	40± 1.00	32± 1.52	26± 1.52

Discussion:

The main aim of this work was to develop oral films to release the drug at oral cavity for immediate release. HPMC 3cps and PVA were selected as film forming polymers

Drug Content and Physical Evaluation:

The assayed drug content in various formulations varied between 93 and 99% (96.48%) average weight of the film was found to be between 859mg and 1050 mg (mean 934 mg) and thickness of the films for all the formulations was found to be between 0.18mm and 0.39 mm with average of 0.26mm.

Table: 7 Evaluation for moisture loss, moisture absorption, % Elongation, tensile strength of oral thin films of cetirizine.

Formulation	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
% Moisture loss	2.89± 0.036	2.71± 0.015	2.58± 0.015	2.52± 0.020	2.44± 0.005	2.34± 0.020	1.83± 0.026	1.53± 0.036
%Moisture absorption	4.17± 0.032	3.95± 0.025	3.84± 0.023	3.73± 0.030	3.65± 0.015	3.54± 0.020	3.43± 0.036	3.24± 0.020
%Elongation	19.45± 0.050	18.90± 0.100	17.93± 0.050	16.83± 0.150	15.93± 0.050	14.50± 0.001	12.50± 0.100	10.93± 0.050
Tensile strength (kg/cm^2)	181.45± 0.54	141.13± 0.28	120.97± 0.47	120.16± 0.12	100.8± 0.24	80.65± 0.63	79.48± 0.32	72.16± 0.23

Table: 8 *In-vitro* dissolution data for oral thin films formulation of cetirizine

TIME (Min)	0	0.5	1	2	5	10	15	20	25	30
F1	0	2.14	3.47	5.52	7.29	12.56	21.69	34.81	49.53	63.86
F2	0	2.79	3.86	6.91	11.89	24.28	36.53	44.26	65.77	78.32
F3	0	11.71	15.73	21.59	29.89	38.73	49.84	63.45	72.92	84.86
F4	0	15.49	19.99	26.79	34.97	45.84	58.73	66.99	76.81	87.53
F5	0	24.78	37.46	52.86	64.77	78.64	83.45	--	--	--
F6	0	32.24	45.83	57.21	74.68	84.29	88.58	--	--	--
F7	0	39.26	53.86	67.28	81.25	92.56	--	--	--	--
F8	0	52.73	64.37	98.54	--	--	--	--	--	--

The oral films of cetirizine containing varying proportions of polymers were determined with an insight to develop the films without any irritation and other problems. The reason for such findings might be ionization of HPMC 3cps at salivary pH which leads to improved attachment of the device to oral cavity. Film of formulation F1 containing high amounts of HPMC 3cps and PVA showed more time for drug release than films of all other formulations, which might be due to high viscosity of the PVA. All the films are disintegrated within 60 seconds and less than that. Tensile strength was found to be increase d with increasing polymer concentration.

***In-vitro* Drug Release Studies:**

The release rate of Cetirizine increased with decreasing concentration of HPMC 3cps as in F7 and F8 respectively. These findings are in compliance with the ability of HPMC 3cps to form complex which leads to immediate release of drug from the device. HPMC 3cps is more hydrophilic and it can swell rapidly, therefore decrease of HPMC 3cps content improves the drug release in F8.

The maximum cumulative percent release of cetirizine from formulation F8 could be attributed due to ionization of HPMC 3cps at pH environment of the dissolution medium. Ionization of HPMC 3cps leads to the development of negative charges along the backbone of the polymer. Repulsion of like charges uncoils the polymer into an extended structure. The counter ion diffusion inside the gel creates an additional osmotic pressure difference across the gel leading to the high water uptake.

CONCLUSION

The main objective of the study was to formulate and evaluate mouth dissolving film containing cetirizine hydrochloride. HPMC & PVA films were prepared by solvent casting method. Compatibility of cetirizine with polymers was confirmed by FT-IR studies. Eight films were evaluated for weight variation and thickness showed satisfactory results. Tensile strength, percentage elongation and folding endurance of the films were increased with increase in the concentration of polymer due to increase in the elasticity nature of the polymer.

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