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Original Article

Formulation design and optimization of novel fast dissolving tablet of chlorpheniramine maleate by using lyophilization techniques ☆

Vivek Dave *, Renu Bala Yadav, Richa Ahuja, Sachdev Yadav

Department of Pharmacy, Banasthali University, Banasthali, Rajasthan, India

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ABSTRACT

Fast dissolving tablets (FDTs) have received more interest in the pharmaceutical industry for those categories of drug which show slow dissolution and less oral bioavailability. Nowadays various technologies have been developed for FDTs with improved patient compliance and convenience. FDTs tablets provide an advantage particularly for the pediatric and geriatric patients who have difficulty in swallowing and also for that who are travelling for a long and suffers from lack of water availability. Lyophilization (freeze-drying) is a process in which water is sublimated from the product after freezing at a specific temperature and pressure. Lyophilization technique is used in order to improve the dissolution of the given substance and improve the oral bioavailability of the drugs with poor solubility and high permeability. In this work, chlorpheniramine maleate FDTs was formulated by lyophilization method. The prepared tablets were subjected to various evaluation such as hardness (2.4–2.9 kg/cm^2), friability (0.68–0.79%), disintegration time (10–19 s), drug content (95.32–99.09%), water absorption ratio (31–53%), wetting time (64–106 s) and *in-vitro* drug release shown in 5 min (96.04–99.92%). FTIR studies showed that there is no interaction between drug and polymer. Stability studies showed that there is no change in drug content within three and six months. Results revealed that fast dissolving tablets of chlorpheniramine maleate prepared by lyophilization method result in rapid dissolution.

1. Introduction

Fast dissolving tablets are tablets which disintegrate and dissolve rapidly in saliva within seconds even if water is not available. From all drug delivery technology, oral route is the best route for taking therapeutic agents. The reasons behind this are accurate dosing, self medication, avoidance of pain, patient compliance, low cost. According to European pharmacopoeia, fast dissolving tablets are those which disintegrate on tongue before swallowing and it should disperse in less than 3 min [1–7]. Dosage forms such as tablets and capsules are being utilized most commonly but dysphasia and difficulty in swallowing are their drawbacks. To overcome these problems, mouth dissolving tablets have developed which are known as novel solid dosage forms and come under novel drug delivery system. Chlorpheniramine maleate (CPM) is used as drug which is incorporated in these fast dissolving tablets prepared by lyophilization techniques method. Chlorpheniramine maleate is an antihistaminic agent which helps in relieving symptoms of allergy, hay fever, cold rashes, watery eyes, itchy eyes, cough, runny nose, sneezing and also it is used in itching of chicken pox. Chlorpheniramine maleate blocks a natural substance known as histamine which is made by our body during an allergic reaction. It also blocks acetylcholine and helps in drying of some body fluids. It also helps in relieving symptoms such as watery eyes, runny nose etc. FDTs are quickly soluble in water, well absorbed and thus dissolves within seconds and good absorbed. Thus, FDT acts like a tablet which dissolves as well as being absorbed very fast. Chlorpheniramine maleate shows first-pass metabolism and its metabolites are desmethyl and di-diesmethylchlorpheamine which decreases its bioavailability. But fast dissolving tablets avoid first pass metabolism and enhance bioavailability of drug. Thus these tablets undergo rapid dissolution within seconds and faster action within minutes. There are various techniques for formulating fast dissolving tablets such as lyophilization, direct compression, tablet molding, sublimation, and lyophilization techniques etc. Elderly people experiences deterioration of their physiological and physical abilities. As per European pharmacopoeia, "Fast dissolving tablets are uncoated tablets placed in the mouth resulting in their dispersion rapidly before being swallowed".

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* Corresponding author at: Department of Pharmacy, Banasthali University, Banasthali, Rajasthan 304022, India.
E-mail address: vivekdave1984@gmail.com (V. Dave).

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Hence in the present study, fast dissolving tablets of chlorpheniramine maleate were prepared by lyophilization techniques method and superdisintegrants such as croscarmellose sodium, crospovidone have been utilized for faster disintegration. The advantages of these tablets are patient compliance, increased bioavailability, rapid onset of action, convenience in administration, good mouth feel etc. [4–6].

2. Materials and methods

2.1. Materials & components

CPM was obtained from MP biomedicals, Mumbai, India, PEG 6000 and PEG 4000 were obtained from HiMedia Pvt. Ltd., Mumbai, India, mannitol was obtained from Central Drug House Pvt. Ltd., Mumbai, India, and microcrystalline cellulose, gelatin & PVP K30 were obtained from Merck, India. All other reagents and chemicals used were of analytical grade.

2.2. Formulation method of FDTs by lyophilization techniques

In this study, FDTs containing Gelatin and Microcrystalline cellulose were prepared by lyophilization techniques method according to the formulae given in Table 1. To prepare different batches, all ingredients (except gelatin and glycine) according to the formula were accurately weighed and passed through 60 and 100 mesh sieve and mixed geometrically. Gelatin was soaked in water, and hydrated gelatin was stirred onto a magnetic stirrer until a clear phase was obtained, an equal proportion of glycine and given amount of mannitol was added to prevent shrinking of gelatin during manufacturing. An accurately weighed amount of Chlorpheniramine maleate (500 mg) was dispersed in the prepared aqueous solution and stirred on magnetic stirrer to obtained a continuous homogenous phase that result in dose of 50 mg Chlorpheniramine maleate FDTs when it was molded to 1 × 10 poly vinyl chloride (PVC) blister pack with a diameter of 13 mm and a depth of 3 mm. These fillings were kept to the deep freezer condition at −20 °C for 24 h. The pre freeze tablet mixtures were placed in lyophilizer (Labconco corporation 8811, 18 lt.) with a condenser temperature of −87 °C (provided by auto cut system) and a pressure of 0.133–0.187 mbar.

The best formulated FDTs were collected and forward to next stage which involved the addition disintegration accelerators namely, PEG 4000, PEG 6000 and Tween 80 to achieved a FDT with good tablet properties [3,11].

2.3. Design of experiment (DOE) for FDTs of Chlorpheniramine maleate by lyophilization method

In this study, an experimental design matrix was formed with 2 factors, 3 level, and 9 runs to optimized the influence of variable by using Statistica V.10 software (StatSoft, Inc. USA). In this matrix design independent variable such as (A) percent of gelatin conc. and (B) percent of PVP K30 conc. were selected and their impact on formulation was predicted. All these dependent variable is summarized in Table 2. On the behalf of this design set goals, 10 FDT formulation were prepared and characterized for *in-vitro* drug release (R1), disintegration time (R2), water absorption ratio (R3), and wetting time (R4) which were taken as a dependent variable (response parameters) [2].

Table 2
Variables and their constraints in Box-Behnken design.

Variables	Constraints	
	Lower limit	Upper limit
Independent variables		
(A) = Percent of gelatin conc.	0.25	0.75
(B) = Percent of PVP K 30	0.50	1.00
Dependent variables	**Goals**	
(R1) = *In-vitro* drug release	Maximize	
(R2) = Disintegration time	Minimize	
(R3) = Water absorption ratio	Optimize	
(R4) = Wetting Time	Minimize	

2.4. Measurement of tablet tensile strength and friability

The ability to withstand mechanical shock of handling in manufacturing, packaging and shipping is measured in terms of tensile strength or crushing load and friability. The crushing load for FDTs of various batches was determined by compressing the tablets in diametric direction using a Pfizer tablet hardness tester (Cadmach, India). The friability of tablets was determined using Roche friabilator USP test apparatus (Electrolab, Mumbai). Randomly six FDTs were chosen from each batch and their initial weight was determined Table 3. The FDTs were placed in friabilator and rotated at 25 rpm for 4 min. They were then removed, dusted and their final weight was determined [14–16,19–23]. The formula for calculating friability is given as Eq. (1):

$$F = \frac{W_i - W_f}{W_i} \times 100 \quad (1)$$

where W_i is initial weight and W_f is the final weight of the tablets.

2.5. Weight variation and tablet thickness

Twenty tablets were randomly taken from each batch and the weight of their average weight was determined. Then individual tablet was taken and its weight was calculated. That individual weight was compared with average weight. The weights were measured using weighing balance [18]. Twenty tablets were randomly selected from formulations and thickness was measured individually by screw gauge. The results were expressed in millimeters Table 3.

Table 1
Formulation table of Chlorpheniramine maleate by lyophilization method.

Ingredients	Formulations									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Chlorpheniramine maleate(mg)	50	50	50	50	50	50	50	50	50	50
Gelatin (mg)	–	–	0.25	0.5	0.75	0.75	0.75	0.75	0.5	0.25
Mannitol (mg)	97.25	97.25	95.75	94.25	96	94.75	93.75	96	93.5	93.25
Glycine (mg)	8.75	8.75	8.75	8.75	8.75	8.75	8.75	8.75	8.75	8.75
Microcrystalline cellulose(mg)	90	92	90	92	90	90	90	90	92	92
PVPK30 (mg)	–	–	0.5	0.5	0.5	0.75	1	0.5	0.5	0.75
PEG6000 (mg)	3	1	3	2	1	2	1	1	_	_
PEG4000 (mg)	_	_	1	2	3	3	4	2	4	4
Tween 80(%w/v)	1	1	0.75	_	0.75	0.75	0.75	1	0.75	1
Total (mg)	250	250	250	250	250	250	250	250	250	250

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Table 3
Evaluation of fast dissolving tablet by lyophilization method.

Test	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Wt. variation (mg)	249 ± 0.05	245 ± 0.08	244 ± 0.15	240 ± 0.02	239 ± 0.32	238 ± 0.87	237 ± 0.21	244 ± 0.58	237 ± 0.55	236 ± 0.21
Hardness (kg/cm^2)	2.0 ± 0.45	2.1 ± 0.21	2.9 ± 0.22	2.5 ± 0.21	2.0 ± 0.22	2.4 ± 0.32	2.0 ± 036	2.1 ± 0.33	2.9 ± 0.38	2.8 ± 0.39
Friability (%)	0.78 ± 0.08	0.69 ± 0.22	0.15 ± 0.24	0.18 ± 0.01	0.26 ± 0.01	0.54 ± 0.6	0.55 ± 0.03	0.32 ± 0.02	0.36 ± 004	0.57 ± 0.36
Thickness (mm)	7.01	6.34	7.96	8.21	8.12	7.88	7.56	7.96	7.23	8.74
Drug content (%)	93	94	97	94	89.57	92	91	96	95	95

2.6. Measurement of disintegration time

The *in-vitro* disintegration time of formulated FDTs was determined using digital disintegration apparatus (Electrolab, Mumbai, India) using 900 ml of pH 6.8 phosphate buffer at 37 ± 0.5 °C. Six tablets from each batch were randomly chosen and the average time for complete disintegration of these tablets was determined Table 3 [13]. All FDTs under test took 16–19 s to disintegrate completely. This quick disintegration time was achieved as a result of using lyophilization technique [8–12,47].

2.7. Wetting time and water absorption ratio

To determine the wetting time of FDTs, a piece of tissue paper was taken and it was folded twice and placed in culture dish (d = 6.5 cm) containing about 6 ml of purified water. An FDTs having small amount of amaranth powder on upper surface was placed on tissue paper. The time elapsed in developing red color on upper surface of the FDTs was determined and noted. To determine the water absorption ratio, the wetted tablets were transferred to a tissue paper and wiped off any excess water and weighed immediately [14–16]. Results are presented in Table 3. The water absorption ratio was calculated by following formula given as Eq. (2):

$$R = \frac{W_a - W_b}{W_b} \times 100 \quad (2)$$

where $W_b$is the weight of tablet before study and W_a is the weight of tablet after study [48].

2.8. Drug content of lyophilized FDTs

Three tablets were randomly chosen from each batch, crushed and the blend equivalent to 5.0 mg of CPM was accurately weighed and transferred to 100 ml volumetric flask. Phosphate buffer (pH 6.8), 20 ml was added under continuous stirring and volume was made up to 100 ml with the same. The solutions were filtered and analyzed spectrophotometrically at 261 nm [20]. Measurements were performed in triplicate.

2.9. Fourier transform infrared (FTIR) spectroscopy

The FT-IR spectroscopy of pure drug CPM, the solid admixture of drug and various excipients in 1:1 ratio used in the formulations as well as the FDTs were characterized by KBr pellet method using Perkin Elmer FTIR Series model-1615spectrophotometer to know the compatibility and interactions. The FTIR spectra are shown in (Fig. 1). The FTIR study did not show any possible interaction between CPM and other excipients used in the fast dissolving tablets.

2.10. Scanning electron microscopy (SEM)

The scanning electron microscopy was used to determine the morphological appearance of the formulated FDTs. The coating of FDTs was done using gold for 10 min with the use of fine coat ion-sputter and examined under FE-SEM (JSM 6701; JEOL, Japan). Signals of electron-sample interactions reveal information about sample including crystalline structure, chemical composition, external morphology etc. A variety of signals at the surface of solid specimens were recorded (Fig. 2a, b). The data was collected from FDTs and 2-dimensional images were generated that displayed spatial variations in these properties.

2.11. Differential scanning colorimetry (DSC)

DSC (NETZSCH DSC 204-F1 Phoenix, U.S.) thermograms of pure drug CPM, excipients used in formulations and FDTs is presented in (Fig. 3). DSC provides information regarding the physical properties like degree of drug crystallinity and amorphous nature of the samples. Approximately 2–4 mg of sample was taken in an aluminium pan which was heated at a scanning rate of 20°/min for a temperature of −50 to 220 °C. The peak area of melting endotherm was used for calculating heat of lyophilization techniques. The *Proteus* software provided with the instrument was used to calculate the thermal peaks [15].

2.12. Thermogravimetric analysis (TGA)

TGA is a technique which helps in monitoring function of temperature or time as sample is subjected to controlled temperature program in a controlled atmosphere. It is a technique in which upon heating a material, its weight increases or decreases [9]. TGA of CPM and excipients is shown in (Fig. 4).

2.13. In-vitro drug release studies

The *in-vitro* dissolution studies of the formulated FDTs were studied in USP dissolution apparatus type II (Tab Machines, Mumbai, India) with a paddle stirrer at 100 rpm filled with 900 ml pH 6.8 phosphate buffer at 37 ± 0.5 °C. FDTs were placed in basket and program was set for a duration of five minutes. Aliquots of dissolution media (2 ml) were withdrawn initially and after every 1 min and replaced with fresh dissolution media. The samples were filtered through a 0.45μ filter membrane (Millipore, County Cork, Ireland) and absorbance was measured spectrophotometrically at λ_{max} 261 nm [17]. The dissolution test was carried out in triplicate and are presented in (Fig. 5).

2.14. Response surface methodology

Response surface methodology (RSM) has proved to be useful statistical and mathematical technique in modeling and process optimization of experimental variables which influences relevant responses and the objective of this research is to optimize these responses [24]. RSM explores the relationships between several independent variables (factors) and one or more dependent variables (responses) [25]. This design is very flexible and suitable for modeling possible curvature in the response functions and constructing second order polynomial models moreover a third level for a continuous factor facilitates investigation of quadratic relationship between the response and each of the factors (NIST/

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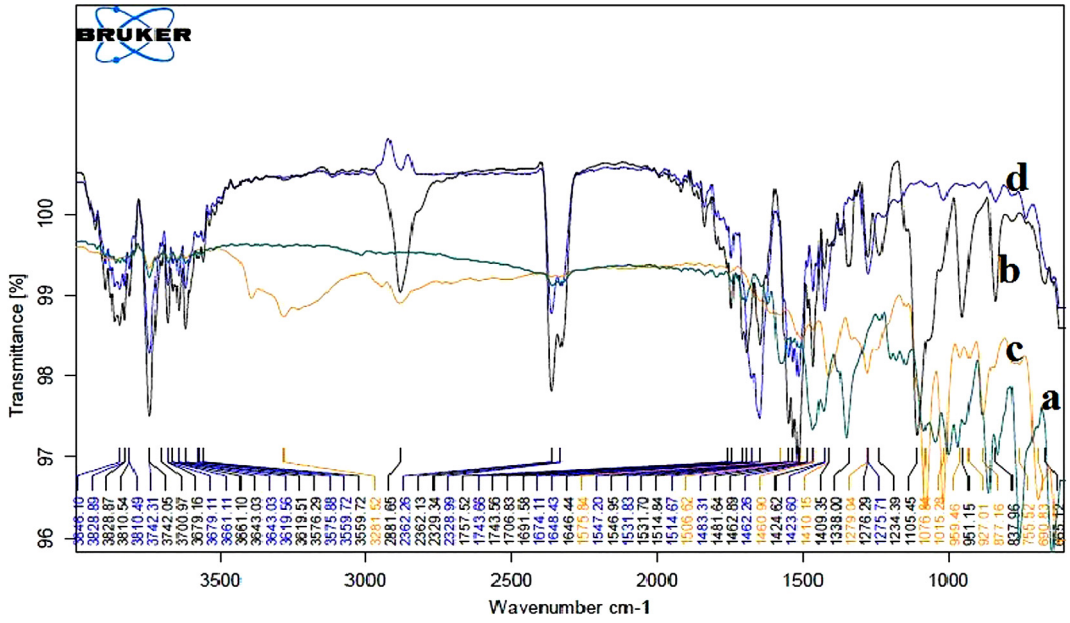

Fig. 1. ATR-FTIR Spectra of the (a) Pure drug, (b) Gelatin, (c) Physical Mixture, (D) PVP K_{30}.

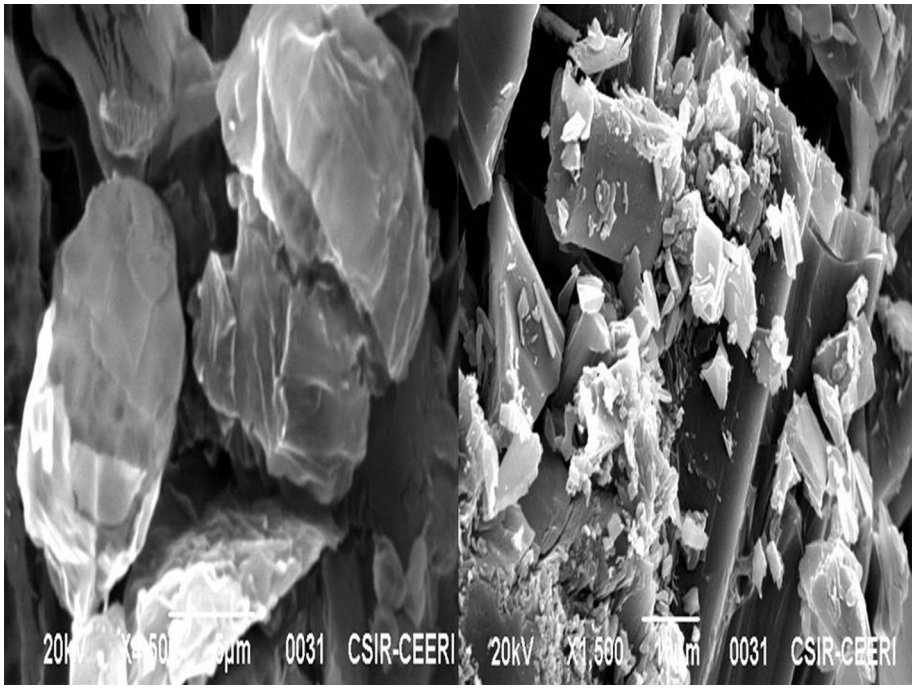

Fig. 2. SEM micrograph of formulated FDT's (a) at x4500 (b) at x5000.

SEMATECH 2015). Ten FDTs formulations were prepared and the effect of independent variables on responses (dependent factors) were evaluated using RSM [26] and are presented in (Fig. 6). Two independent variables were selected: the content of Gelatin (*CP*, X_1) and PVP K30 (*CM*, X_2) and each variable was tested at different concentrations, the quantities of which are expressed in their respective units. The responses evaluated were: drug dissolution (*%DR*, R_1), disintegration time (*DT*, R_2), and water absorption ratio (*WAR*, R_3) and wetting time (*WT*, R_4). Experiments were performed according to a randomized procedure and the scheme showing the values of process variables corresponding to the observed responses is reported in Table 4. Statistica V.10_software (StatSoft, Inc. USA) was used for generation and evaluation of response surfaces.

2.15. Stability studies

The capability of dosage form to continue with its physical, chemical, therapeutic and toxicological specifications is known as stability. For evaluation of dosage forms, stability is an important tool which provides information regarding acceptance or rejection of these dosage forms [20,21].

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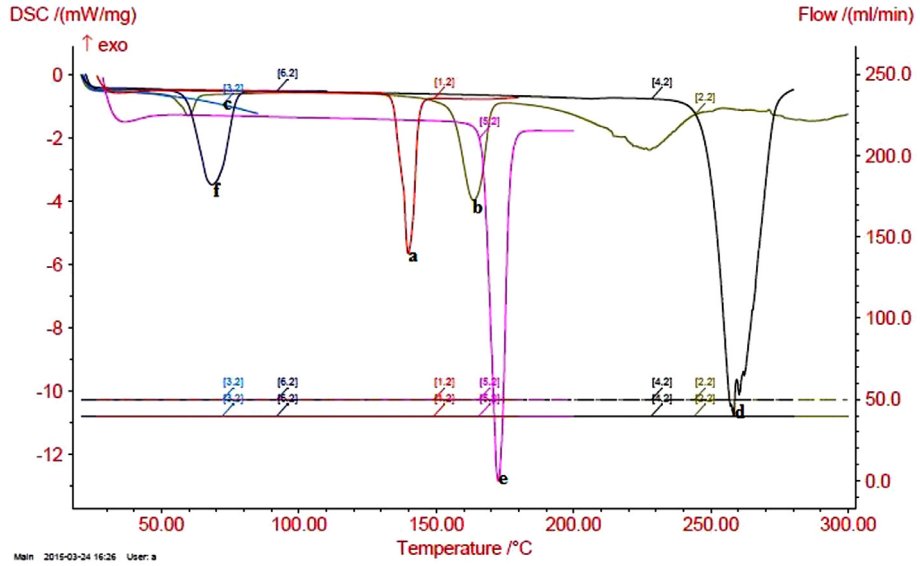

Fig. 3. Combined DSC thermogram of (a) Pure drug, (b) Optimized formulation, (c) Gelatin, (d) Glycine, (e) Manitol, (f) PEG 6000.

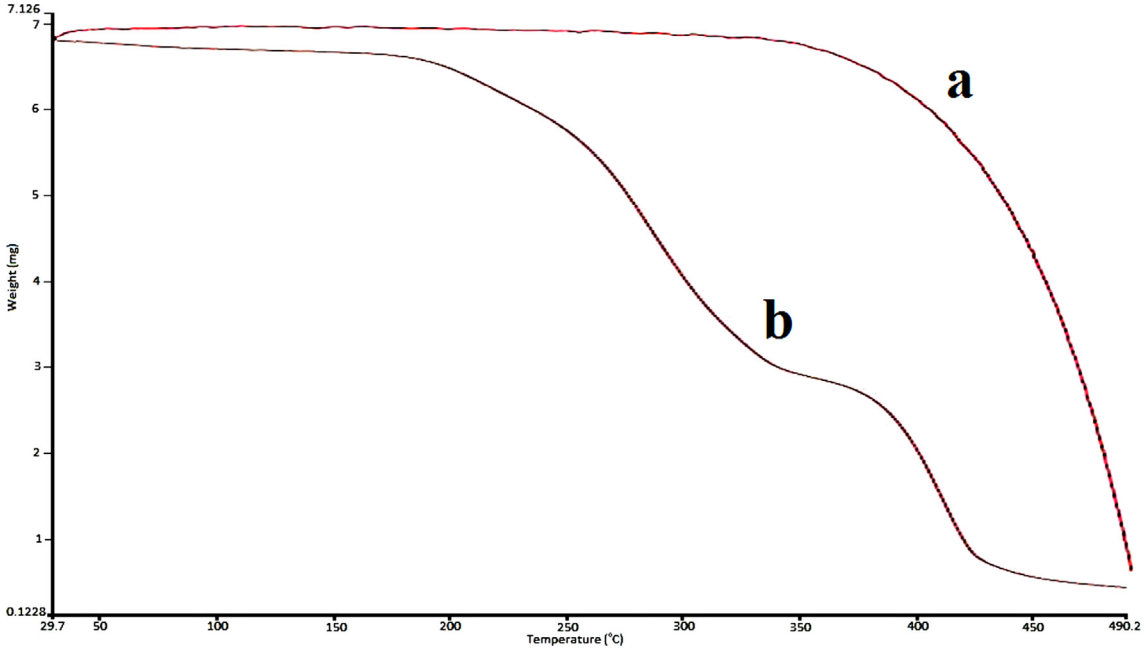

Fig. 4. TGA of a) pure drug CPM, b) formulated FDT's.

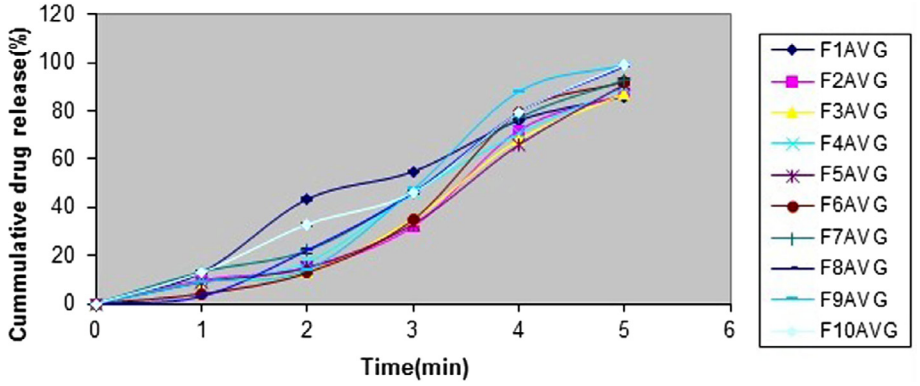

Fig. 5. Dissolution graph of formulated FDT's.

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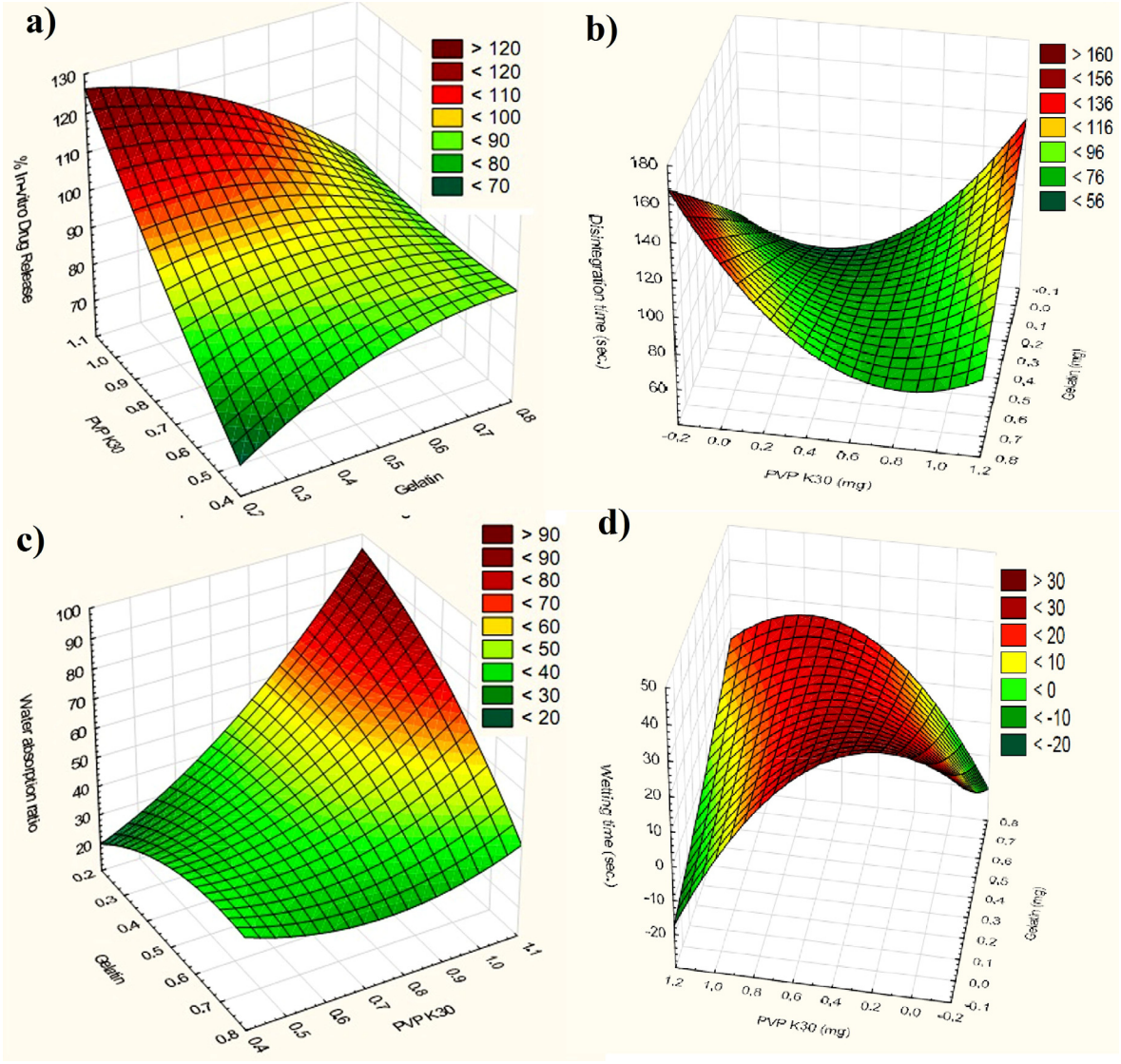

Fig. 6. Response surface plots showing effect of concentration of Gelatin and PVP K_{30} on measured responses (a) *In-vitro* Drug Release (%), (b) Disintegration time (s), (c) Water absorption ratio, (d) Wetting time (s).

Table 4
Process variables and their corresponding measured responses.

Batch	Gelatin (mg)	PVP K30 (mg)	*In-vitro* drug release (%)	Disintegration time (s)	Water absorption ratio	Wetting time (s)
F1	–	–	64.67 ± 1.60	34 ± 1.1	26 ± 1.12	64 ± 1.3
F2	–	–	72.09 ± 0.67	31 ± 1.35	28 ± 1.34	67 ± 1.5
F3	0.25	0.5	78.78 ± 1.49	29 ± 1.08	29 ± 1.40	69 ± 8.7
F4	0.5	0.5	81.56 ± 1.07	27 ± 1.42	30 ± 1.20	74 ± 8.5
F5	0.75	0.5	86.23 ± 0.89	25 ± 1.12	32 ± 1.09	78 ± 8.5
F6	0.75	0.75	90.12 ± 0.2	24 ± 1.4	36 ± 1.59	74 ± 8.5
F7	0.75	1	92.23 ± 0.35	23 ± 1.32	43 ± 2.01	76 ± 8.6
F8	0.75	0.5	93.23 ± 2.13	22 ± 1.21	45 ± 2.06	85 ± 5.6
F9	0.5	0.5	95.45 ± 2.36	21 ± 1.02	48 ± 2.46	78 ± 8.3
F10	0.25	0.75	96.85 ± 2.76	20 ± 0.08	49 ± 3.01	77 ± 4.5

3. Results and discussion

3.1. Fourier transform infrared spectroscopy

The pure drug CPM and solid admixture of drug and various excipients with formulation were characterized by FTIR spectroscopy for testing compatibility of CPM with its polymers and formulation. The IR transmission spectra of drug, polymers and formulation are given in (Fig. 1). All the peaks were present in their original position which shows that there is no drug-carrier interaction. The characteristic peak of CPM is 2350.92 cm^{-1} due to its amino group i.e. N—H stretching. Other characteristic peaks present were 1580 cm^{-1} (C=C stretching), 1475 cm^{-1} (C=H stretching), 864 cm^{-1} (C—C stretching), 1352 cm^{-1} (C—C bending),

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1697.92 cm^{-1} (—C═O stretching), 1576.69 cm^{-1} (C—N stretching), 702 cm^{-1} (C—Cl stretching). Similarly, the polymer used in formulation showed its characteristic peaks which are separate from drug which showed that drug is compatible with polymer and leads to good stability.

3.2. Scanning electron microscope

The change in morphological appearance of drug was studied using scanning electron microscopy. The SEM micrographs (Fig. 2) showed that presence of excipients such as Microcrystalline cellulose, PVP K30, PEG600 and PEG 4000 influence the surface morphology of FDTs and pure drug. The surface morphology of FDTs demonstrated hard but rough and fragmented fibrous network like structures. Several regions on surface showed randomly scattered cubical particles of drug whereas excipients showed rough material structures.

3.3. Differential scanning calorimetry

The DSC thermogram (Fig. 3) of pure drug CPM shows sharp endothermic peak at 139 °C indicating its melting point. The glass transition of CPM was 41.04 °C. There is lack of drug peak in the thermogram of FDTs showing that CPM was completely dissolved with the excipients and is present partially in crystalline and partially as molecular distribution. The thermograms of microcrystalline cellulose and mannitol indicated their melting points at 300 °C and 83 °C respectively and were according to their melting range. There was lack of glass transition temperature in thermogram of any excipients and also in FDTs.

3.4. Thermogravimetric analysis

In this analysis, the drug CPM and formulated FDTs were subjected to controlled temperature program in a controlled atmosphere. In TGA graph of CPM (Fig. 4) showed that the mass remained constant with increasing temperature but as it approached melting point of drug, the mass started to decrease. The thermogram of FDTs showed three endotherms which are probably the melting points of CPM at 139 °C, Gelatin peak at 60 °C, Glycine at 70 °C, mannitol peak at 175 °C and PEG 6000 peak at 260 °C which revealed that excipients or moisture content have no adverse effect on formulations.

3.5. Disintegration testing

The disintegration data of the FDTs is shown in Table 4. The FDTs formulation F1 and F6 showed slow disintegration of 19 s. Whereas faster disintegration rate of 16 s was observed in FDTs (F9) containing gelatin quantity of 0.5 mg that is necessary for lyophilization and hence the formulation became more porous which lead to decrease in the disintegration time.

3.6. In-vitro dissolution studies

The *in-vitro* dissolution studies of the formulated FDTs were performed to evaluate the effect of Gelatin and microcrystalline cellulose on release pattern of CPM (Fig. 5). The dissolution rate of FDTs without Gelatin and microcrystalline cellulose was extremely slow. Only about 19.8% drug was released in 1 min and 64.67% drug was released in 5 min. But when the ingredient was lyophilized by using gelatin and glycine upon varying conc. then drug release reached 90.21% (F10) in 5 min. The above results indicate that FDTs containing 0.5 mg gelatin 4 mg of PEG4000 and 0.75 mg of Tween 80 are the most optimized formulation in respect of CPM release.

3.7. Response surface analysis

The response surface models fit between the factors and measured responses is shown in the equations given below:

$$\%\ \text{In-vitro Drug Release} = 11.895 + 160.62X + 90.44Y - 68X^2 - 141.44XY + 13.76Y^2$$

$$\text{Disintegration Time} = 65.4548 + 89.68.93X - 48.8136Y - 4.4068X^2 - 122.1921XY + 86.4859Y^2$$

$$\text{Water absorption ratio} = -25.5 + 193X + 30Y - 84X^2 - 180XY + 76Y^2$$

$$\text{Wetting Time} = 32.6638 - 51.2486X + 20.9492Y + 8.4746X^2 + 69.4463XY - 50.0113Y^2$$

The response surface plots representing the relationship between the studied factors and measured responses are demonstrated in (Fig. 6).

The different batches of FDTs were prepared by lyophilization method using gelatin and PVP K30 also in different excipient concentrations and all formulations were evaluated [27–48]. Total of 10 formulations with different concentrations of excipients and fixed concentration of drug were evaluated. Weight variation of all formulations was observed in range of 236 to 240 mg which was within acceptable limit for uncoated tablets as per USP. FDTs (batch F1 to F10) showed weight variation, thickness of 6.84–8.72 mm, drug content of 89.57 to 97%, water absorption ratio of 26 to 49%, wetting time of 64–85 sec and *in-vitro* drug release showed 64.67 to 96.85% within 5 min. The best optimized formulations (F9 and F10) showed best results from all formulations. In both, F10 is the most optimized formulation which showed disintegration time of 20 s. All the formulations were evaluated using different evaluation parameters. First evaluation parameter was weight variation which was performed with all 10 formulations. Weight variation was observed within the acceptable limits for FDTs as per USP. The primary requirement of FDTs is rapid disintegration. Angle of repose (θ) determines the internal friction and cohesion of particles. If value of angle of repose is higher, then it shows greater cohesiveness of powder but if its value is low, it shows non-cohesiveness of powder. All formulations showed good to acceptable flow properties as indicated by values of angle of repose (30.31–39.28). Carr's index showed values up to 20 which denote acceptable to good flow ability. All formulations had Hausner's ratio values within the stated limit. If the crushing strength (hardness) of FDTs is higher, it takes longer time to disintegrate. So the most important factor in formulation of FDTs is their mechanical integrity. The hardness of tablets was found to be in the range of 2.1–2.9 kg/cm^2 and friability was observed between 0.44 to 0.69% which were also within acceptable limits. The disintegration time was observed between 20–34 s. Disintegration test showed that formulations in which gelatin and PVP K30 were used in optimized conc. showed rapid disintegration. But formulation in which gelatin was added in quantity more than 0.5 mg showed longer disintegration. This is due to rapid uptake of water from the medium. Due to swelling disintegration time decreases. Thus, the most optimized formulation containing 0.25 mg Gelatin, 0.75 mg PVP K30 showed rapid disintegration. Percentage drug content and wetting time were also observed which were found to be within acceptable limits. It was found that in case of optimized formulation 32.12% drug was released in first 2 min. But in five minutes, about 96.85% of drug was released. Thus, lyophilization played the most important role in enhancing drug

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Table 5
Stability study data of FDTs by lyophilization method.

S. No.	Month (days)	Stability conditions	Condition values*	Release in 5 min (%)	
				(F9)*	(F10)*
1.	30	Room temperature	(25 ± 2 °C/60 ± 5% RH)	90.91 ± 0.81	92.85 ± 0.26
		Accelerated temperature	(40 ± 2 °C/75 ± 5% RH)	80.02 ± 0.71	80.44 ± 0.76
		Cool temperature	(4 ± 2 °C/65 ± 5% RH)	87.99 ± 0.12	86.06 ± 0.85
2.	60	Room temperature	(25 ± 2 °C/60 ± 5% RH)	89.01 ± 1.63	90.45 ± 0.85
		Accelerated Temperature	(40 ± 2 °C/75 ± 5% RH)	79.06 ± 0.77	79.66 ± 0.47
		Cool temperature	(4 ± 2 °C/65 ± 5% RH)	86.02 ± 0.70	84.46 ± 0.89

* All data expressed as mean ± S.D.; n = 3.

release. Thus formulation 10 was considered the best formulation. Now the FT-IR spectra showed that there is no interaction between CPM and other excipients. Thus, it could be concluded that the lyophilization based FDTs of CPM showed fast disintegration, quick drug release and faster onset of action.

3.8. Stability studies

The stability studies were carried out according to ICH guidelines for three and six month at room temperature 25 ± 2 °C/60 ± 5% RH, accelerated temperature 40 ± 2 °C/75 ± 5% RH, and cool temperature 4 ± 2 °C/65 ± 5% RH. The tablets were withdrawn after a period of 30 and 60 days and analyzed for drug release within 5 min. Results are presented in Table 5. According to the observation it was observed that the sample stored at room temperature were shown a satisfactory drug release after a storage time of 30 and 60 days i.e. optimized formulation F9, 90.91 ± 0.81% and 89.01 ± 1.63% and formulation F10, 92.85 ± 0.26% and 90.45 ± 0.85% respectively. While, the samples stored at accelerated and cool temperature, results in decrease in% drug release. Hence, we can concluded that room temperature is suitable for the storage condition of Chlorpheniramine maleate FDT. All the analysis were carried out in triplicate and the results are reported as mean ± SD.

4. Conclusion

From the above work it was concluded that the lyophilized formulation of the CPM was found to be more feasible than the conventional one, the water soluble ingredient used in the formulation were increases the water solubility of the drug. As we know that the CPM possess the problem of oral bioavailability, by making the use of lyophilized CPM the oral bioavailability may enhanced up to its require limit. Here in the present work the use of Gelatin and PVP K30 at the conc. 0.5 and 0.75% give the good formulation drug release with better mechanical strength, thus we can say that a lyophilized product of CPM may achieve good formulation capability for pharmaceutical manufacturer by using these ingredients.

Declaration of interest

The authors report no conflict of interest.

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