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Research Article

Formulation and Evaluation of Chlorpheniramine Maleate Mouth Dissolving Films

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ABSTRACT

The present investigation was aimed at preparation and evaluation of mouth dissolving films (MDFs) of an anti-histamine drug, Chlorpheniramine Maleate (CPM) to enhance convenience and compliance to the elderly and paediatric patients. The MDFs were prepared using wet film applicator and evaluated for physicochemical and physicomechanical properties. MDFs were prepared with 0.6% and 0.8% w/w CPM. The MDFs with 0.8% w/w drug load showed re-crystallisation within 10 days, while the MDFs with 0.6% w/w CPM load were transparent with no re-crystallization. The effect of film formers, film thickness, film modifiers, saliva stimulating and soothing agents on the physicomechanical properties and CPM release from MDFs were evaluated. MDFs casted at 30mil thickness containing poly ethylene glycol (PEG-400) as plasticizer showed superior CPM release rates along with good physicomechanical properties. MDFs with hydroxy propyl methyl cellulose (HPMC) E3 as film former gave superior CPM release rate when compared to E5 and E15 formulations. MDFs with poly vinyl pyrrolidone K30 (PVPK30) gave superior drug release properties when compared to MDFs without PVP K30. The MDFs with citric acid (CA) and xylitol gave superior CPM release than the other MDFs. Release kinetics data reveals diffusion as drug release mechanism.

Keywords: Chlorpheniramine maleate, Mouth dissolving films, Wet film applicator, HPMC**Article Info:** Received 02 Jan 2019; Review Completed 08 Feb 2019; Accepted 09 Feb 2019; Available online 15 Feb 2019**Cite this article as:**Teja D, Jasvanth E, Mounika B, Nalluri BN, Formulation and Evaluation of Chlorpheniramine Maleate Mouth Dissolving Films, Journal of Drug Delivery and Therapeutics. 2019; 9(1-s):244-251 DOI: <http://dx.doi.org/10.22270/jddt.v9i1-s.2417>***Address for Correspondence:**

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INTRODUCTION

As a site for drug delivery, oral cavity (intraoral route) offers advantages over the conventional gastro-intestinal route, the parenteral and other mucosal routes of drug administration. It provides direct entry into the systemic circulation thereby avoiding the hepatic first pass effect with ease of administration and the ability to terminate drug delivery when required ¹. Recent developments in the technology have presented viable dosage alternatives from oral route for paediatrics, geriatric, bedridden, nauseous or noncompliant patients ². Buccal drug delivery has lately become an important route of drug administration. Various bio adhesive mucosal dosage forms have been developed, which includes adhesive tablets, gels, ointments, patches and more recently the use of polymeric films for buccal delivery, also known as mouth dissolving films ³. Mouth dissolving films (MDFs), a new and novel drug delivery system for per oral delivery of the drugs, were developed based on the technology of the transferral patch. MDFs have gained popularity due to its availability in various sizes and shapes. The film is placed on the top or the floor of the tongue ⁴. When put on the tongue, this film disintegrates instantaneously, releasing the drug which dissolves in the

saliva. Some drugs are absorbed from the mouth, pharynx, and oesophagus as the saliva passes down into the stomach. In such cases, the bioavailability of the drug is significantly greater than that observed for conventional tablets ⁵.

Chlorpheniramine Maleate (CPM) is a histamine H1 antagonist and indicated for the treatment of hay fever, common cold, rhinitis, urticaria, allergic reactions, and asthma ⁶. CPM is used in the treatment of allergy act by competing with histamine for H1-receptor sites on effector cells. They thereby prevent, but do not reverse, responses mediated by histamine alone. CPM undergoes first pass metabolism and has an oral bioavailability of 25-50% ⁷. It is available in syrup, tablet, sprays and lozenge forms and is available in the market as over-the-counter drugs named Cadistin, Cepiam TR, Chloram, Cipium, etc. Keeping in view the patient compliance and the need for better therapeutic efficacy the present investigation was aimed at the preparation and evaluation of CPM MDFs and to ensure quick onset of action.

Few reports were published on the formulation and evaluation of CPM MDFs and none of them were developed and evaluated systematically. In most of the works reported so far, MDFs were prepared in petri plates, moulds, etc. and

the films were dried at 40-45°C overnight and this procedure may not result in uniformity in thickness and drug content and thereby vary the drug release rates⁸⁻¹⁰. Moreover, no works on the influence formulation variables like film thickness, polymer viscosities, surfactants and saliva stimulating agents were reported. MDFs were not evaluated thoroughly for the drug loading effect on the crystallization and characterization studies. Hence, the present investigation was aimed to prepare CPM MDFs using wet film applicator, an industrially scalable technique and evaluate them systematically keeping in view all the above parameters.

MATERIALS AND METHODS

Materials

CPM was obtained from Aurobindo India Ltd., Hyderabad. HMPc E3, E5, E15 were obtained from Colorcon Asia Ltd., India. Ethanol, PVP K30 and SLS were purchased from Loba Chemie, Mumbai. Xylitol was purchased from Roquette laboratories, France. Pine apple flavour was obtained from Darwin laboratories, Vijayawada. All the ingredients of analytical grade were used.

Preparation of Artificial Saliva

Artificial saliva was prepared by dissolving sodium chloride-0.844g; potassium chloride-1.2g; calcium chloride dihydrate-0.193g; magnesium chloride hexahydrate-0.111g and potassium phosphate dibasic-0.342g were added one by one to 500mL of distilled water and then the volume was made up to 1000 mL using the distilled water. The pH was adjusted with 0.1N HCl to 5.7¹¹.

Preparation of CPM MDFs

CPM MDFs were prepared as per formulae given in Table 1 to a batch size of 5g. Drug was dissolved in a mixture of solvents (water and ethanol) in a beaker and other ingredients were added one by one and finally polymer hydroxy propyl methyl cellulose (HPMC) was added and mixed thoroughly. The mixture was sonicated for 5 minutes to remove entrapped air bubbles and casted on a glass plate with a wet film applicator set at 30 mil (750µm) and 40 mil (1000µm) and it was dried at 45°C for 60min in hot air oven. Then the dried films were peeled off from the glass plate, cut into appropriate sizes, and stored in desiccators until use.

HPLC analysis of CPM

Chromatographic Conditions

An HPLC System (Shimadzu) comprising of a Degasser (DGu-20A3), Binary pump (LC- 20 AD), an Auto-sampler (SIL- 20 AC HT) and a PDA-detector (SPD M20A) was used to develop method for analysis of CPM in samples. LC solution software was used to collect and process the data. Mobile phase consisting of 0.02% Formic acid: Methanol (68:32 v/v) at used at a flow rate of 1mL/min. For quantitative analytical purpose 10µL of the samples were injected and the eluents were monitored at 220nm and the separation was achieved at an ambient temperature. Under these LC conditions the CPM was eluted at 4.8 min.

Fourier transform infrared spectroscopic Analysis (FTIR):

Samples were analysed using an ATR-FTIR spectrometer (Bruker, Germany) and the powder or film sample was simply placed onto the ATR crystal and the sample spectrum was collected. ATR spectra were measured over the wave number range of 4000-500 cm⁻¹ at a resolution of 1.0 cm⁻¹.

Evaluation Parameters for CPM MDFs

Morphological Properties

The films were packed in aluminium foil pouches and were stored at room temperature (25 ± 3°C) with relative humidity of approximately 65 ± 5% and were tested periodically every month for a period of 6 months. Properties such as homogeneity, colour, transparency, and surface of CPM MDFs were tested visually.

Thickness

The thickness of film was evaluated using a screw gauge with a range of 0-10mm and revolution 0.001 mm. Anvil of the thickness gauge was turned and the film was inserted after making sure that the pointer was set to zero¹⁵⁻¹⁷. The film was held on the anvil and the reading on the dial was noted down. The estimations were carried out in triplicate.

Drug Content

One cm² film was taken in a 10mL volumetric flask and dissolved in 5mL of artificial saliva and then final volume was made up with artificial saliva. Samples were suitably diluted with artificial saliva and were analysed. The estimations were carried out in triplicate.

Variation of Mass

Mass of one cm² film from different batches of the formulations was noted and the estimations were carried out in triplicate.

In Vitro Disintegration Studies

In MDFs the disintegration and dissolution procedures are hardly distinguishable. If the MDF disintegrates it concurrently dissolves in a small amount of saliva which makes it difficult to mimic these natural conditions and measures with an adequate method. In the present investigation two methods of disintegration were adopted to mimic natural conditions.

Drop Method

In this method, the films were placed on a glass slide and placed planar on a petri dish. One drop of distilled water was dropped by a pipette onto the oral films¹⁵⁻¹⁷. The time until the film dissolves and forms a hole in the film was measured. The estimations were carried out in triplicate.

Petri dish Method

In this method 2mL of distilled water was placed in a petri dish and a film of 2x2 cm² was placed on the surface of the water and the time required to dissolve the film completely was measured. The estimations were carried out in triplicate.

Tensile Strength

Tensile strength is the maximum stress applied to a point at which the film specimen breaks

[12]. It is calculated by the load at rupture divided by the cross-sectional area of the film as given below:

$$\text{Tensile strength} = \frac{\text{Load at Failure} \times 100}{\text{Film Thickness} \times \text{Film Width}}$$

Tensile strength of MDFs was measured using Mini Tech Tensiometer-UTM9051 (Dak Systems Inc., Mumbai, India) fitted with a load cell of 500N (50kg) capacity and the data was collected using Test Bench II software¹⁵⁻¹⁷. Samples of appropriate film thickness with fixed dimensions (LxW-10*2cm) were fixed between pneumatic grips with a gauge dimension of 3cm length between grips. All the dimensions were entered into software to calculate the cross-sectional

area. The film was carefully placed in between the pneumatic grips without any loose folds. Instrument was operated at speed of 5mm/min until the film breaks. Percent elongation data was also computed from the software for each sample. Whole experiment was carried out in triplicate.

Percent Elongation

When stress is applied the film sample stretches and is referred to as strain. Strain is basically the deformation of the film divided by the original dimension of the film. Generally, elongation of the film increases as the plasticizer concentration increases¹³. Percentage elongation was calculated by measuring the increase in length of the film after tensile strength measurement by using the following formula.

$$\text{Percent Elongation} = \frac{[L - L_0] \times 100}{L_0}$$

Where, L = Final length, L₀ = initial length.

Percent elongation was computed from the Test bench II software for tensile strength measurement. The estimations were carried out in triplicate.

Folding Endurance

Folding endurance is determined by repeated folding of the film at the same place till the film breaks. This gives an indication of brittleness of the film. The number of times the film is folded without breaking is computed as the folding endurance value¹⁴. The estimations were carried out in triplicate.

In Vitro Drug Release Studies

The *in vitro* drug release studies were conducted using 500mL of artificial saliva as dissolution medium with modified USP Type V Dissolution Rate Testing Apparatus. A temperature of 37°C and 50 rpm were maintained. Each film of appropriate size (3.4x 3.4cm²) equivalent to 4mg dose was cut and placed on a watch glass covered with nylon wire mesh. The watch glass was then dropped into dissolution flask. 2mL samples were withdrawn at predetermined time intervals 2, 5, 10, 20, 30, 40, 50, 60, 80, 100, 120, 180, 240,

300sec and every time replaced with 2mL of fresh dissolution medium. The samples were analysed using HPLC method. The drug release experiments were conducted in triplicate.

Stability Studies

Stability studies were carried out on F9 containing 0.6% w/w of CPM and HPMC E3. The MDFs were packed in aluminium pouches, sealed and stored at 40°C /75 ± 5% RH for 6 months. The appearance, weight and drug content properties of the MDFs were examined.

Statistical Analysis

Results of experimental data were subjected to one-way ANOVA (using Fisher's LSD Post HOC test) using SYSTAT software (SYSTAT Software Inc., San Jose, USA). Results with 'p' value of less than 0.05 were considered as of significant variance.

RESULTS AND DISCUSSION

Preparation and Physical Characterization of CPM MDFs

In the present investigation the MDFs were prepared using a wet film applicator of the ease of removal and quick drying of the films, which is also a commercially scalable technique.

Initially placebo MDFs were prepared using different polymers like HPMC E3, HPMC E5, HPMC E15, methyl cellulose and sodium carboxy methyl cellulose (NaCMC), using PEG-400 as plasticizer. The MDFs were observed for their film forming capacity and their appearance. Finally, from the trails made and results obtained, HPMC E3, HPMC E5 and HPMC E15 were selected for further development. Initially MDFs were prepared with CPM load of 0.8% using water-ethanol as solvents, and the films were casted at 30 mil thickness. However, crystallization was observed within a period of 10 days. Hence further trials were made with CPM load of 0.6 % and the films were casted at 30 mil and 40 mil thickness. The MDFs were transparent with no crystallization and all the formulae were given in Table 1.A 5g batch size of formulations were given approximately 88.16 cm² film area.

Table 1: Composition of different CPM MDFs

Ingredients (mg)	Formulae (5g batch size)										
	F1	F2	F2A*	F3	F4	F5	F6	F7	F8	F9	F10
CPM	40	30	30	30	30	30	30	30	30	30	30
HPMC E3	375	375	375	-	-	375	375	-	-	375	-
HPMC E5	-	-	-	375	-	-	-	375	375	-	375
HPMC E15	-	-	-	-	375	-	-	-	-	-	-
PVP K30	-	-	-	-	-	2	-	2	-	2	2
SLS	-	-	-	-	-	-	2	-	2	-	-
PEG 400*	25	25	25	25	25	25	25	25	25	25	25
Water*	1785	1785	1785	1785	1785	1785	1785	1785	1785	1785	1785
Ethanol*	2730	2740	2740	2740	2740	2738	2738	2738	2738	2725.5	2725.5
Citric acid	-	-	-	-	-	-	-	-	-	12.5	12.5
Colouring agent	10	10	10	10	10	10	10	10	10	10	10
Flavouring agent	10	10	10	10	10	10	10	10	10	10	10
Xylitol	25	25	25	25	25	25	25	25	25	25	25

*All the amounts were taken based up on their density.

FTIR Analysis

The CPM showed characteristic peaks at 1577.78cm⁻¹(aromatic amine bending), 2967.11cm⁻¹ (C-H bending), 1739.17cm⁻¹(C=O stretching), 1621.30cm⁻¹(C=C stretching), 1351.33 cm⁻¹(C-N stretching), 756.15 cm⁻¹ (C-Cl bending).

These characteristic peaks of CPM were all retained in the MDFs. These characteristic peaks of CPM were all retained in the MDFs. These results indicate that there is no interaction between CPM and excipients in MDFs. The FT-IR spectrums of CPM were shown in Fig 1.

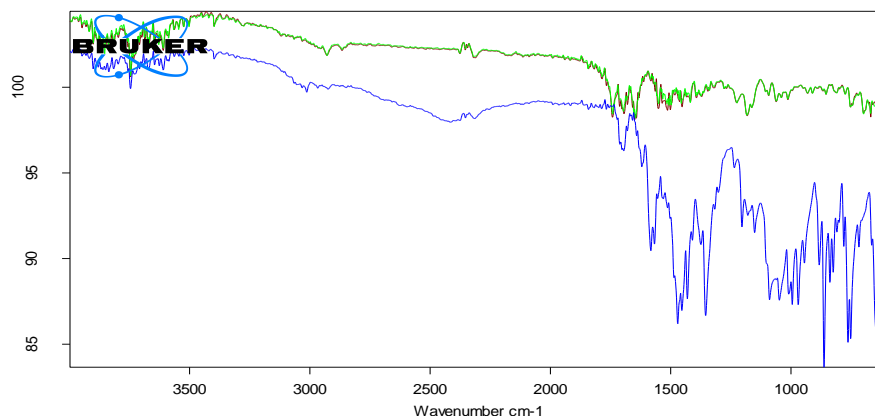


Figure 1: FTIR Spectra for pure CPM(—), F9 (---) and F10 (···)

Morphological properties

CPM MDFs were visually tested for homogeneity, transparency, colour and smoothness. MDFs formulated with 0.8% w/w CPM were transparent initially but turned opaque within 10 days and is due to crystallization of CPM. MDFs

with 0.6% CPM showed no change in properties even at the end of 6 month time period and no crystallization of CPM was observed. The photographs were shown in Fig.2. The morphological characterization of MDFs was further established by visualizing MDFs under binocular microscope (Olympus-CH20i) with magnification 10x.

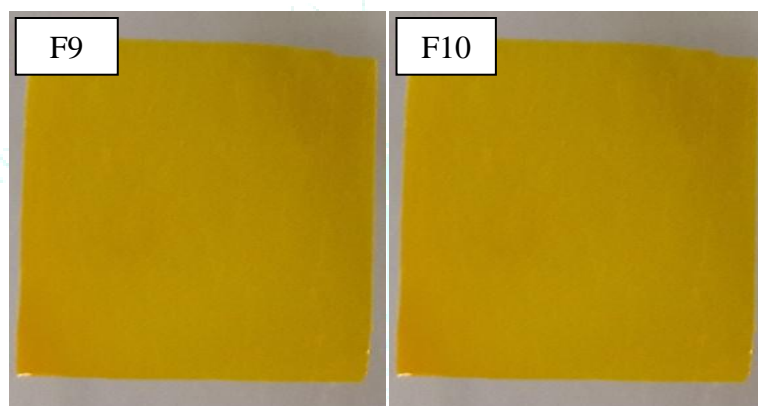


Figure 2: Photographs of CPM MDFs

Thickness

The thickness was measured with screw gauge at different places of MDFs in order to evaluate the reproducibility of preparation method. Around 90% of wet film thickness was

lost during drying. The results were given in Table 2 and a good uniformity of thickness was observed. MDFs casted at 40 mil thickness and MDFs with PVP and SLS showed higher thickness values compared to other formulations.

Table 2: Physico-mechanical properties of different CPM MDFs

Formulations	Drug content (mg/cm ²) (n=3)	Mass variation (mg) (n=3)	Thickness (μm) (n=6)	Disintegration time(sec)	
				Drop method (n=3)	Petri dish method (n=3)
F2	0.39 ± 0.01	2.60 ± 0.26	73.33 ± 5.16	12.33 ± 0.57	22.33 ± 1.58
F2A	0.41 ± 0.02	2.73 ± 0.05	83.33 ± 5.16	17.33 ± 0.57	27.00 ± 1.58
F3	0.39 ± 0.02	2.53 ± 0.05	78.33 ± 4.08	14.66 ± 0.57	23.66 ± 1.15
F4	0.37 ± 0.01	2.86 ± 0.05	93.33 ± 5.16	16.00 ± 0.00	24.66 ± 0.58
F5	0.39 ± 0.03	2.80 ± 0.10	78.33 ± 4.08	11.00 ± 1.00	19.66 ± 1.15
F6	0.38 ± 0.02	2.63 ± 0.23	76.66 ± 5.16	11.33 ± 1.15	21.33 ± 1.73
F7	0.39 ± 0.02	2.73 ± 0.05	85.00 ± 5.47	13.33 ± 0.57	20.33 ± 0.58
F8	0.38 ± 0.03	2.63 ± 0.15	85.33 ± 5.16	14.33 ± 0.57	21.33 ± 0.57
F9	0.40 ± 0.02	2.96 ± 0.05	81.66 ± 4.08	10.33 ± 0.57	18.33 ± 1.58
F10	0.40 ± 0.02	2.93 ± 0.15	86.66 ± 5.16	12.33 ± 0.57	19.33 ± 0.58

Drug content

Films of 1 cm² were cut from different places (n=3) of whole film and CPM content was estimated. The results were given in Table 2. The results indicated a good uniformity of CPM within the film, overall good solubilisation of CPM in MDFs was observed. MDFs casted at 40mil thickness gave higher CPM content values compared to MDFs casted at 30mil thickness which may be due to decrease in film area obtained with 30mil thickness.

Variation of mass

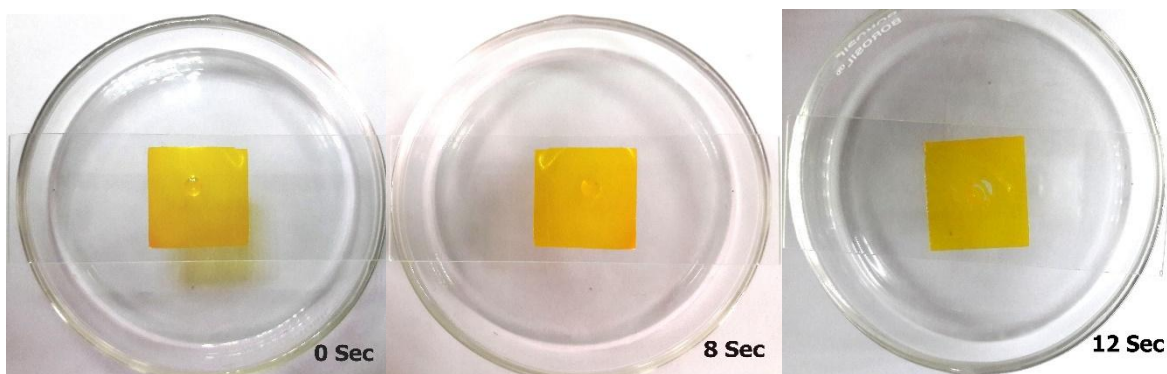
Films of 1 cm² were cut from different batches and weighed. The results are given in Table 2. Same mass of film was

obtained with three batches of films indicating reproducibility of preparation method and formulation.

In Vitro Disintegration Studies

The results of disintegration time are given in Table 2. The results indicated that HPMC E3 formulations disintegrated faster than the E5, E15 which is due to low viscosity of E3 polymer compared to E5 and E15. The CPM MDFs casted at 30mil showed faster disintegration rates compared to those casted at 40mil. The MDFs with PVP K30 disintegrated faster than the MDFs without PVP K30. The MDFs with CA and xylitol showed faster disintegration compared to the other formulations. The images of MDF (F9) disintegration by drop and petridish methods are shown in Fig. 4.

A)



B)

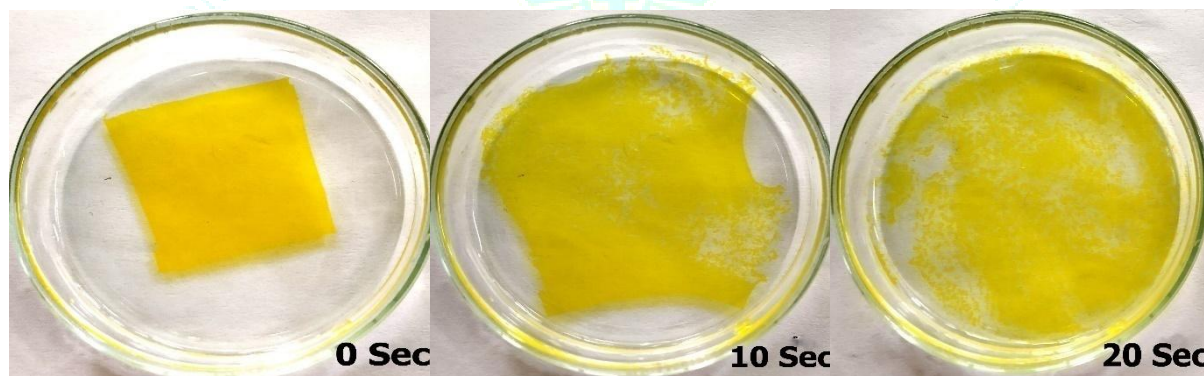


Figure 4: *In vitro* disintegration of CPM MDFs by A) Drop method B) Petri dish method

Tensile Strength and % Elongation

MDFs should possess moderate tensile strength and % elongation. The results revealed that all films showed

moderate tensile strength values. With the increase in the viscosity of the polymer the tensile strength of the MDF has increased. The results were given in Table 3 and shown in Fig 5.

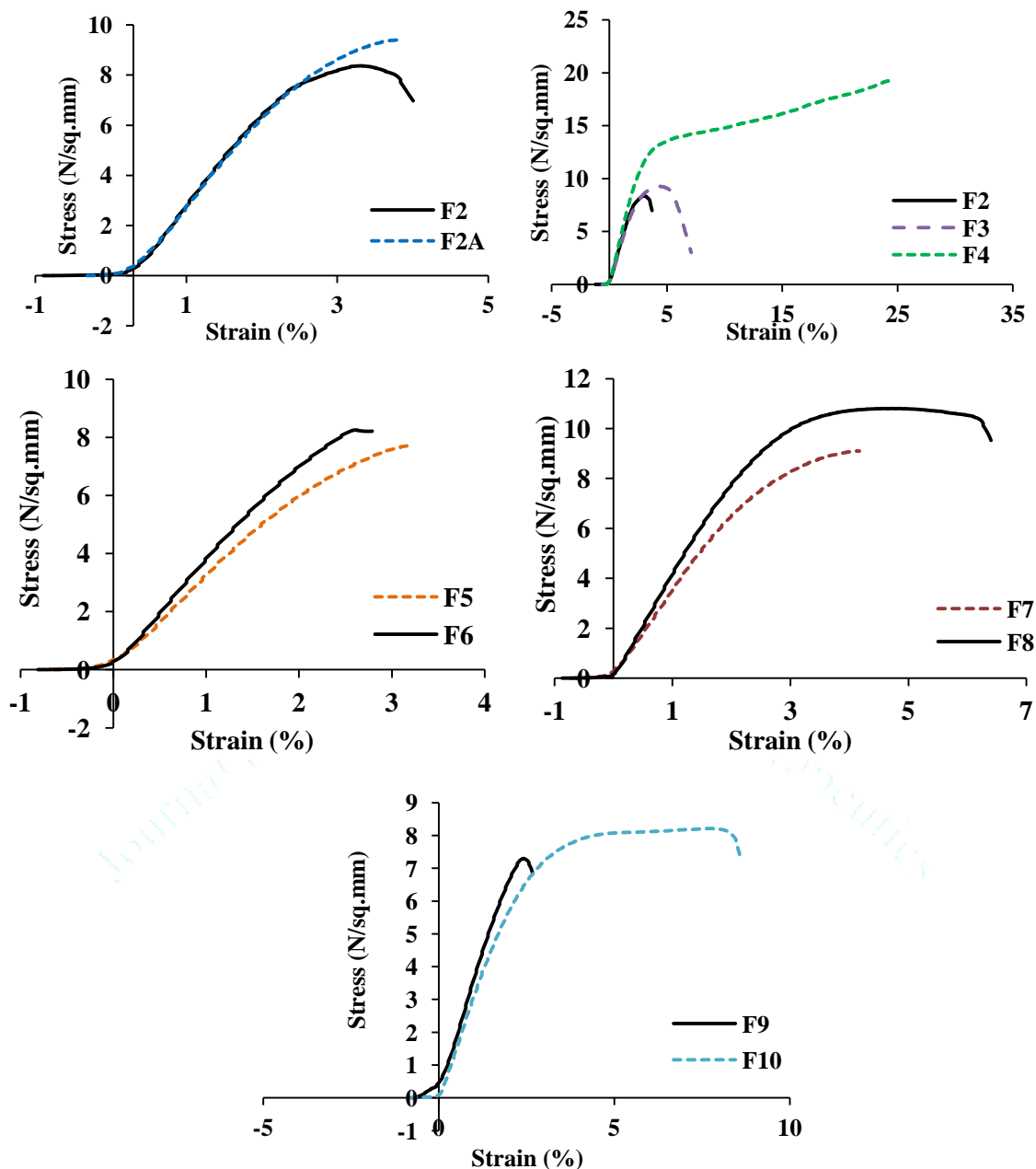


Figure 5: Comparative Tensile Strength Profiles of CPM MDFs

Table 3: Physico-mechanical properties of different CPM MDFs

Formulations	%Elongation	Folding endurance
F2	4.50 ± 0.16	97
F2A	4.89 ± 0.05	88
F3	4.66 ± 0.05	94
F4	5.70 ± 0.26	90
F5	5.23 ± 0.11	105
F6	5.25 ± 0.25	102
F7	4.80 ± 0.16	101
F8	5.23 ± 0.20	99
F9	5.24 ± 0.11	117
F10	5.33 ± 0.11	113

Folding Endurance

The MDFs prepared with HPMC polymer showed good folding endurance. MDFs casted at 40 mil thickness showed low folding endurance values compared to other formulations. The results were given in Table 3.

In Vitro Drug Release Studies

In the present investigation, drug release of MDFs was carried out using USP Type-V dissolution rate testing apparatus. 500mL of artificial saliva was used as dissolution medium in order to mimic the *in vivo* conditions. The *in vitro* drug release profiles of CPM MDFs are shown in Fig. 6.

Initially to study the effect of film thickness on the release rates of CPM from MDFs, formulations were prepared using HPMC E3 as film forming agent, PEG-400 as plasticizer and films were casted at 30 mil and 40 mil thickness. 30mg of CPM (0.6% w/w drug load) was added in each formulation. The cumulative percent of CPM released at the end of 5 secs is 41.89± 5.89 and 45.76 ± 4.77 for F2 and F2A respectively. Complete CPM release was obtained at 40s and 60s for F2 and F2A respectively.

From the results obtained, it was found that the formulations casted at 30 mil thickness (F2) gave superior results compared to formulations casted at 40 mil thickness (F2A). An increase in thickness of the MDFs (as in case of 40 mil

thickness) has resulted in delayed disintegration of films which in turn has delayed the drug release from the MDFs. This indicates that the release of drug from MDFs is affected by the film thickness. Hence the MDFs with 30 mil thickness have been selected for the further investigation.

The studies were continued to evaluate the effect of polymer viscosities on the rate of CPM release from the MDFs. Formulations (F2, F3 and F4) were casted at 30 mil thickness and using PEG-400 as plasticizer and HPMC E3, E5 and E15 as film formers. 30mg of CPM (0.6% drug load) was added to each formulation. The cumulative percent of CPM released at the end of 5sec is 41.89 ± 5.88 , 34.62 ± 7.73 and 24.88 ± 5.27 for formulation F2, F3 and F4 respectively. The complete release of CPM was obtained at 40sec, 50sec and 60sec respectively. The release rate of F2 is significantly higher than the F3 and F4 formulations. This can be due to the lower viscosity of the HPMC E3 polymer. With an increase in the viscosity of the polymer the release of the CPM from MDF has decreased significantly. Overall, the order of percent of CPM released from the MDFs is $F2 > F3 > F4$.

The formulations containing HPMC E3 and E5 were selected to study the effect of solubilising and/or wetting agents on the release of CPM. PVP K30 and SLS were added to the formulations at a level of 0.04% (2mg). Cumulative percent of CPM released at the end of 5sec is 51.51 ± 3.36 and 47.44 ± 0.85 for formulation F5 (E3 with PVP K30) and F6 (E3 with SLS) respectively, while 50.57 ± 3.13 % and 49.6 ± 1.51 % of CPM release was observed for formulation F7 (E5 with PVP

K30) and F8 (E5 with SLS) respectively. The complete release of CPM was obtained at 30sec, 40sec, 50sec and 50sec for F5, F6, F7 and F8 formulations respectively.

The MDFs with PVP K30 and SLS showed significantly superior drug release profiles when compared to the MDFs without PVP K30 and SLS. The MDFs with PVP K30 showed superior drug release profiles when compared to the films with and without SLS. The MDFs with HPMC E3 as film forming agent and PVP K30 showed superior results when compared to the MDFs with HPMC E5 and PVP K30. Overall the MDFs with PVP K30 showed superior drug release profiles when compared to the other formulations.

The effect of saliva stimulating agents and soothing agents on the release rates of CPM from the MDFs was also studied. CA and xylitol were added to the formulations at 0.25% and 0.5% levels respectively. Cumulative percent CPM release from the MDFs at the end of 5sec was 76.38 ± 2.63 for formulation F9 containing HPMC E3 with PVP K30, CA and xylitol; and 70.12 ± 1.24 for F10 formulation containing HPMC E5 with PVP K30, CA and xylitol. The complete release of CPM from the MDFs was obtained at 20sec and 40sec for F9 and F10 formulations respectively. The MDF formulations with CA and xylitol showed superior CPM release when compared to the other formulations. The formulation F9 was optimized because of its CPM release profile, physicomechanical, physicochemical, *in vitro* disintegration and *in vitro* drug release properties when compared to the other formulations.

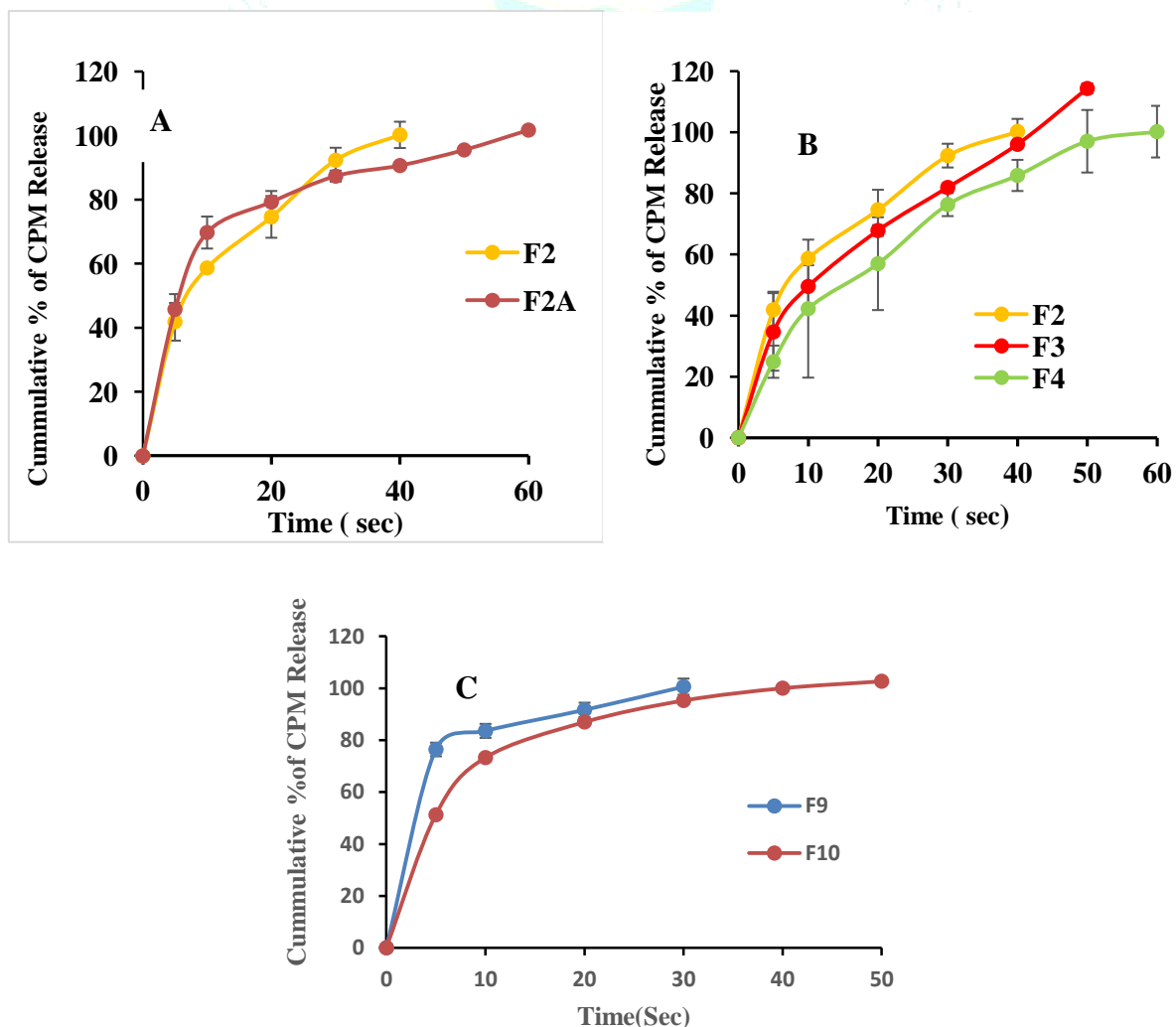


Figure 6: Effect of (A) Thickness (B) Polymer viscosity (C) Solubilizing and Saliva stimulating agents on *in vitro* CPM release from MDFs

Drug release kinetics

To understand the release profiles obtained with CPM MDF formulations, the drug release data obtained at different time points was fitted into kinetic models such as First Order [18], Higuchi model [19]. The first order release rate constant 'k' (sec⁻¹) values and Correlation Coefficient (R²) values calculated from drug release data (0-300 sec) for CPM MDFs.

When compared to F2, a 1.15 and 1.9 fold decrease was observed with F3 and F4 formulations respectively. When compared to F2, the 'k' values were higher for F5 & F6 containing PVP K30 & SLS. A 2.18 fold and 1.17 fold increase was observed for F5 & F6 formulations respectively when compared to F2 formulation. When compared to F3, the 'k' values were higher for F7 & F8 containing PVP K30 & SLS. A 2.35 fold and 1.89 fold increase was observed for F7 & F8 formulations respectively when compared to F4 formulation. A 1.04 fold increase in 'k' values was obtained for formulation F9 (E3, PVP K30 & CA) when compared to F5 (E3 and PVP K30); while a 3.27 fold increase in 'k' values was obtained for formulation F10 (E5, PVP K30 & CA) when compared to F7 (E5 and PVP K30). A 1.65 fold increase was observed for F9 formulation containing E3 with PVP K30 and CA when compared to F10 (E5 with PVP K30 & CA).

Overall, MDFs with CA and PVP K30 gave higher 'k' values when compared to MDFs without CA and PVP K30. MDFs with PVP and SLS gave higher 'k' values compared to MDFs without PVP and SLS. MDFs with PVP gave higher 'k' values than SLS. The Higuchi square root model of all MDFs showed good correlation coefficient values (0.814-0.976) indicating diffusion as release mechanism.

Stability Studies:

Stability studies were carried out for F9 formulation containing 0.6% w/w CPM with HPMC E3. MDFs were stored at 40°C with relative humidity of approximately 75 ± 5% for 6 months. The appearance, weight variation and drug content of the MDFs were examined. The appearance of MDFs remained unchanged throughout the studies and no crystallization was observed. There is no statistically significant change observed in weight of MDFs. F9 showed 96-103% of CPM content after 6 months, indicating that the CPM was stable in MDFs.

CONCLUSIONS

From this investigation, it can be concluded that CPM can be successfully formulated into MDFs. The film properties and drug release rates can be affected by the formulation variables such as film thickness and polymer viscosities and percent drug loading. The casting films with wet film applicator resulted in CPM MDFs with reproducible physico-mechanical and physicochemical properties from batch to batch. MDFs casted with 30mil thickness containing PEG-400 showed good physico-mechanical properties along with superior CPM release rates compared to other formulations. Formulation F9 was subjected to stability studies and no change in appearance, weight and drug content was observed indicating that the CPM was stable in the formulations. Formulation F9 (0.6% w/w CPM, 7.5 % w/w HPMC E3, 0.5 % w/w PEG-400, 0.04 % w/w PVP K30, 0.25% CA and 0.5% xylitol) showed better physico-mechanical and drug release properties when compared to remaining formulations. The administration of CPM as MDFs may provide quick onset of action with enhanced oral bioavailability and therapeutic efficacy compared to current marketed formulations like IR and ODT's.

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CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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