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FORMULATION AND EVALUATION OF MOUTH DISSOLVING FILMS OF LOSARTAN POTASSIUM USING 3^2 FACTORIAL DESIGN

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ABSTRACT: The objective of the present study was to develop mouth dissolving films (MDF) of Losartan potassium for the treatment of hypertension, with fast disintegration, optimum morphological properties, and mechanical strength. Losartan is an anti-hypertensive drug which undergoes extensive first-pass metabolism that results in low bioavailability of the drug. Through buccal route, the drug directly enters blood circulation and hence bioavailability of the drug increases. Hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, sodium alginate, and gelatin were used as the hydrophilic film-forming polymeric bases and glycerol as plasticizer. Films were prepared by solvent casting technique. Parameters like *in-vitro* disintegration time, tensile strength, content uniformity, folding endurance, swelling index, and *in-vitro* drug release were evaluated. 3^2 factorial design was used to optimize the amounts of the polymer and the plasticizer. *In-vitro* dissolution studies showed that 99% of Losartan potassium was released within 5 min with an average disintegration time of 38 sec. UV and FTIR spectrophotometry were used to identify drug-excipient interactions. Accelerated stability studies were performed as per ICH guidelines wherein the MDFs were stable for 2 months at 40 ± 2 °C and 75 ± 5% relative humidity.

INTRODUCTION: Buccal route is an important route of administration for some drugs whose access to the blood is limited by many factors when administered per-oral. Oral mucosa is permeable to a large number of drugs and is largely vascularized which makes it an appropriate route for drug administration and has gained attention since recent years [1, 2]. The drug enters directly into the bloodstream through the oral mucosa, and hence onset of action is rapid compared to per-oral route [3].

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Through buccal route, a drug bypasses the exposure to conditions of GIT and hepatic portal pathway and directly enters the circulation [4]. Since, hepatic pathway is bypassed, first pass metabolism of the drug that affects the final blood drug concentration, is decreased.

Hence, drug delivery through the buccal route is advantageous in increasing bioavailability of the drug and exhibiting fast action [5]. GTN (glyceryl trinitrate) sublingual tablet, recommended for instant relief from chest pain in heart failure is a well-known example that shows fast action through buccal route [6]. In the present work, losartan potassium was selected as a model drug to evaluate mouth dissolving films (MDFs) as an efficient dosage form for direct delivery of the drug into circulation.

These films dissolve within few minutes once put into the mouth and release the drug for quick uptake by buccal mucosa. Losartan potassium is an angiotensin II receptor antagonist used to treat primarily high blood pressure besides other disease conditions [7]. Although, the absorption of Losartan is good after oral administration due to high first-pass metabolism, its bioavailability is reduced to only extensively after per-oral dose [8, 9]. Since, buccal route circumvents the hepatic pathway and delivers the drug directly into the blood circulation Losartan potassium seems to be a good candidate for such evaluation. Many pediatric and geriatric patients find it difficult to swallow solid dosage forms like tablets and capsules. To overcome this problem, fast dissolving oral films were invented in the late 1970s [10]. A fast dissolving film, also known as fast dispersing or mouth dissolving film utilizes a hydrophilic polymer which hydrates and dissolves instantly to release the drug on coming in contact with the contents of the oral cavity [11]. Over the past years, MDFs have emerged as efficient oral care products as dosage forms for delivering vitamins [12], in the form of breath strips, and personal care products [13]. Today fast dissolving films are seen as new options for improved systemic delivery of poorly absorbed drugs as well.

MATERIALS AND METHODS:

Materials: Losartan potassium was received as a gift sample from Eaton laboratories, Srinagar. HPMC was received from Protech Bio-Pharm PVT Ltd., Pulwama. Sodium carboxymethylcellulose was received as a gift sample from Ambrosia Pharmaceuticals, Srinagar. All other excipients were purchased from Central drug house Pvt. Ltd., New Delhi, India.

Methods:

Preparation of Buccal Film: Films were prepared by solvent casting technique. The required quantity of polymer was accurately weighed and allowed to soak in water for 24 h until it formed a uniform viscous solution. Other ingredients *viz*., Glycerol (as plasticizer), SSG (as super-disintegrant), Saccharin sodium (as a sweetener) were added to the polymer solution, and the mixture was sonicated for 2 h to remove any entrapped air. These ingredients were added to modify the drug release properties and mucoadhesion of the buccal films. The drug was dissolved in the dispersion, and the solution was then cast as the film on Petri plates and allowed to dry for 24 h in a hot air oven at 45 ºC. The optimization was carried through a 3^2 factorial design [14].

The preliminary investigation for preparation of films was performed using different polymers including HPMC 5cps, Na-CMC, Na–alginate and Gelatin **Table 1**. The study suggested that HPMC 5cps was most suitable polymer for the preparation of the films **Table 2**.

TABLE 1: COMPOSITION OF MDFS USING DIFFERENT POLYMERS

Ingredients	F_{T1}	F_{T2}	F_{T3}	F_{T4}	F_{T5}	F_{T6}	F_{T7}
HPMC 5cps (% w/w)	45	---	---	---	30	30	30
Na-CMC (% w/w)	---	45	---	---	15	---	---
Na–alginate (% w/w)	---	---	45	---	---	15	---
Gelatin (% w/w)	---	---	---	45	---	---	15
Glycerol (% w/w)	10	10	10	10	10	10	10
SSG (% w/w)	4	4	4	4	4	4	4
Saccharin sodium	5mg	5mg	5mg	5mg	5mg	5mg	5mg
Menthol	0.05 ml	0.05 ml	0.05 ml	0.05 ml	0.05 ml	0.05 ml	0.05 ml
Dist. Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s

TABLE 2: PHYSICAL AND MECHANICAL PROPERTIES OF MDFS

F. code	Visual Appearance	Tack Test	Tensile strength (kg/mm^2)	Folding endurance	Disintegration time
F_{T1}	Transparent	Non-tacky	0.440±0.06	>100	55sec ±1.63
F_{T2}	Semi-Transparent	Non-tacky	0.178±0.03	<100	153sec ±2.54
F_{T3}	Non-Transparent	Non-tacky	0.113±0.05	<50	127sec ±2.60
F_{T4}	Transparent	Slightly-tacky (increased rapidly when exposed to external conditions)	0.107±0.08	<50	368sec ±3.12
F_{T5}	Transparent	Non-tacky	0.193±0.05	<100	133sec ±3.24
F_{T6}	Transparent	Non-tacky	0.156±0.07	<100	105±3.60
F_{T7}	Transparent	Slightly-tacky	0.125±0.09	<50	314sec ±2.90

Experimental Design: 3^2 full factorial design was used for optimization of polymer - plasticizer ratio. In this design, 2 factors were evaluated each at 3 levels, and experimental trials were performed in all 9 possible combinations. The amount of polymer HPMC 5 cps (X1) and amount of plasticizer, glycerol (X2) were selected as independent variables and each factor being studied at -1, 0, +1 level. **Table 3** and **4** give the levels of independent variables used and the full factorial design layout of the variables respectively. The composition of various mouth dissolving films is given in **Table 5**.

TABLE 3: INDEPENDENT VARIABLES DESIGN

Factor	Level used, actual (coded)		
Independent Variables	**Low (-1)**	**Medium (0)**	**High (+1)**
X1 = Concentration of polymer (% w/w)	45%	50%	55%
X_2 = Concentration of plasticizer (% w/w)	10%	15%	20%

TABLE 4: FULL FACTORIAL DESIGN LAYOUT

Formulation Code	Variable Levels	
	X_1 (Polymer)	**X_2 (plasticizer)**
F_1	-1	-1
F_2	-1	0
F_3	-1	+1
F_4	0	-1
F_5	0	0
F_6	0	+1
F_7	+1	-1
F_8	+1	0
F_9	+1	+1

Calculation of the Amount of Drug to be poured per plate:

An oral dose of Losartan potassium = 50 mg
Bioavailability = 33%
Therefore, actual bioavailable dose = 50 × 33/100
= 16.5 mg
Therefore, amount of drug to be loaded per 2 × 2 cm^2 film = 16.5 mg
Area of Petri plate = πr^2
= $3.14 \times (4.75)^2$
= 70.84 cm^2
Therefore, number of films = 70.84/4
= 17.71
Drug amount required = 17.71 × 16.5
= 292.2

TABLE 5: COMPOSITION OF VARIOUS FILMS PREPARED USING 3^2 FULL FACTORIAL DESIGN

Formulation code	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Drug	292mg	292mg	292mg	292mg	292mg	292mg	292mg	292mg	292mg
HPMC 5cps (% w/w)	45%	45%	45%	50%	50%	50%	55%	55%	55%
Glycerol (% w/w)	10%	15%	20%	10%	15%	20%	10%	15%	20%
Saccharin sodium	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg
Sodium starch glycolate (% w/w)	4%	4%	4%	4%	4%	4%	4%	4%	4%
Menthol	0.05ml	0.05ml	0.05ml	0.05ml	0.05ml	0.05ml	0.05ml	0.05ml	0.05ml
Dist. Water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

Morphological Properties of Prepared Films: Properties such as homogeneity, color, transparency, and surface of MDF were tested visually. All the formulations were wrapped in a butter paper and then in aluminum foil, stored at room temperature (25 ºC) with a relative humidity of 65 ± 5% Rh and were tested periodically for 3 months.

Tack Test: Tackiness was evaluated gently by pressing the film between fingertips and results were noted in qualitative terms as tacky or non-tacky.

Thickness Evaluation: It is essential to ascertain uniformity in the thickness of the film as this is directly related to the accuracy of dose distribution in the film. The thickness of the film was measured by calibrated digital Vernier Calipers. The thickness was evaluated at five different locations (four corners and one at center).

Weight Variation: This test was carried out by taking 2 × 2 cm^2 of the film cut at three different places from the casted film. The weight of each film was taken individually using electronic balance. Average of three readings were taken for weight variation study.

Folding Endurance: The folding endurance which is related to the flexibility of a film was measured manually by firmly holding and folding the films repeatedly through the middle. The number of folds on the same crease, required to produce a crack in the film was noted as the value of folding endurance [15].

pH Evaluation: The surface pH of the MDFs was determined to investigate the possible side effects due to change in pH *in-vivo*, since an acidic or alkaline pH may irritate the oral mucosa. The surface pH was determined by using the pH meter.

The film was allowed to swell by keeping it in contact with 1ml of distilled water for 1 h at room temperature. The pH was noted down by bringing the electrode in contact with the surface of the film, allowing it to equilibrate for 1 min and the pH was recorded.

Tensile Strength: The tensile strength of the films was evaluated by using a TAXT Plus Texture Analyzer (Texture Technologies, Scarsdale, NY) and miniature tensile grips TA-96B according to the procedure described below: A 2 × 2 cm^2 film free from air bubbles or physical imperfections was held longitudinally in the tensile grip on texture analyzer. The test was performed at 6 mm of initial grip separation from both sides at a crosshead speed of 2 mm/sec till the film broke [16]. All measurements were conducted in triplicate for each film. **Table 6** gives the parameters set in the instrument before performing the test.

TABLE 6: SETTINGS OF THE TEXTURE ANALYZER

Pre-test speed	1.50 mm/sec
Test speed	2.00 mm/sec
Post-test speed	10.00 mm/sec
Trigger force	5.00 kg
Data acquisition rate	200 pps

In-vitro* Disintegration of Films*: *In-vitro* disintegration time of 2 × 2 cm^2 films was determined visually in a petri dish containing 25 ml of phosphate buffer pH 6.8 at 37.0 ± 0.5 °C. The time when the film started to break or disintegrate was recorded, which is the disintegration time of the film [17, 18].

Percentage Moisture Loss: Percentage moisture loss was calculated to check the integrity of films at the dry condition. Films were cut into 2 × 2 cm^2 and weighed accurately and kept in desiccators containing fused anhydrous calcium chloride. After 72 h the films were removed and weighed again. The decrease in the weight of the films gave the amount of moisture loss. The % age loss in moisture was calculated by using the following formula:

% age moisture loss = (Initial weight - final weight) / (Initial weight) × 100

Percentage Moisture Absorption: The moisture uptake was determined by cutting films into 2 × 2cm^2 patches. These films were put for one day in a desiccator containing a saturated solution of potassium sulphate (relative humidity 75%) at room temperature. The increase in the weight of the films was observed which was due to absorption of moisture. The % age gain in the moisture by the films was calculated using the following formula:

% age moisture loss = (Initial weight - final weight) / (Initial weight) × 100

Swelling Index: A pre-weighed drug loaded film was placed on a 2% agar plate. An increase in the weight of the film was noted until the constant weight was obtained.

Drug Content Uniformity: Drug content of all formulations was determined by UV- spectro-photometric method. For this 2 ×, 2 cm^2 film was cut and dissolved in 100 ml of phosphate buffer pH 6.8. The solution was filtered, and absorbance was

recorded at 206 nm. Drug content was calculated from the calibration curve of the drug. All the readings were taken in triplicate.

***In-vitro* Dissolution and Drug Release Study:** The *in-vitro* dissolution test was carried out in a USP II paddle dissolution apparatus. The films of appropriate size (2 × 2 cm^2) were cut and placed in dissolution media. The dissolution medium consisted of 300 ml freshly prepared phosphate buffer (pH 6.8), maintained at 37 ± 0.5 ºC and stirred at 50 rpm. Samples of 5 ml were withdrawn at predetermined time intervals & replaced with fresh medium. The samples were subjected to UV analysis at 206 nm (λ_{max}) [19].

Surface Morphology Study by SEM (Scanning Electron Microscopy): The surface morphological properties of the pure drug and prepared films were investigated using a scanning electron microscope (Hitachi S-3000). The samples were mounted on an aluminum stub by coating with a thin layer of gold approximately 20 nm in vacuum. The scanning electron microscope was operated on an accelerated voltage and microphotographs were taken at appropriate magnifications.

Accelerated Stability Studies for Optimized Formulation: Accelerated stability studies were carried out according to ICH Q1A (R2) guidelines. The chosen formulations F_3 and F_6 were assessed for accelerated stability study. Each film (2 × 2 cm^2) was wrapped in a butter paper followed by aluminum foil and placed in an aluminum pouch, which was heat-sealed at the end**.** Stability study was carried out at 40 ± 2 °C and 75 ± 5% Rh for 2 months. Samples were withdrawn after 15 days interval and evaluated for physico-chemical properties. The similarity factor was applied to study the effect of storage concerning its physical appearance, *in-vitro* disintegration time, tensile strength and drug content after storing at 40º ± 2º C / 75 ± 5 % Rh for 2 months [20].

Drug-Excipient Interaction Studies: To ascertain that no interaction has occurred between the drug and the polymer or due to conditions of the formulation process, the following interaction studies were carried out.

UV Spectral Analysis*:* In this study, polymers used were blended with the drug. The blend was dissolved in phosphate buffer pH 6.8, filtered and analyzed using UV spectrophotometer. UV spectrum obtained was compared with the UV spectrum of the pure drug.

FTIR Spectral Analysis*:* The FTIR spectra of pure drug, physical mixture and formulation F_3 (after storage at accelerated conditions) were recorded using an FTIR spectrophotometer (Agilent Cary 630). The samples were scanned over a range of 4000-500 cm^{-1}.

RESULTS AND DISCUSSION: The preliminary screening of polymers for the preparation of the MDFs showed that the HPMC 5cps MDFs were transparent with tensile strength, disintegration time and folding endurance in the desired range as compared to the films of Na-CMC, Na-Alginate, and Gelatin.

Morphological Properties of Prepared MDFs: The formulations stored at room temperature (25ºC) with the relative humidity of approximately 65 ± 5% Rh showed no change in the properties at the end of 3 months; especially no crystallization of the drug was observed.

Tack Test: Films F1 to F8 were non-tacky. The F9 was slightly tacky. This may be due to a higher percentage of hydrophilic polymer and hydrophilic plasticizer which have a higher tendency to retain moisture **Table 7**.

Thickness Evaluation: It is essential to ascertain uniformity in the thickness of the film as this is directly related to the accuracy of dose distribution in the film**.** The thickness of the films gradually increased with increase in the amount of the polymer and was found in the range of 0.07 to 0.09 mm **Table 7**.

Weight Variation: All the batches were uniform in weight with no significant difference in the weight of the individual formulations from the average value. Weight variation was found to be in the range of 0.082 ± 0.002 to 0.189 ± 0.006 mg for films prepared **Table 7**.

Folding Endurance: The folding endurance of different MDFs was in the range of 100 to 250 as shown in **Table 7**. Folding endurance of films increased with increase in the concentration of

HPMC and glycerin. This could be due to more elasticity of polymer at higher levels of HPMC in the films and also as the plasticizer concentration increases, the flexibility of the film also increases with consequent increase in folding endurance **Table 7**.

pH Evaluation: The surface pH of the MDFs was determined to investigate the possible side effects due to change in pH *in-vivo*, since an acidic or alkaline pH may irritate the oral mucosa. The surface pH was determined by using the pH meter. The surface pH of formulated MDFs was found to be in the range of 6.1 to 7.5 **Table 7** which indicated that the formulated MDFs were in the neutral pH range and would not cause any irritation after placing in the oral cavity.

Percentage Moisture Loss: Percentage moisture loss was calculated to check the integrity of films at the dry condition. Films were cut into 2 × 2 cm^2 and weighed accurately and kept in desiccators containing fused anhydrous calcium chloride. After 72 h the films were removed and reweighed. Percentage moisture loss was inversely proportional to the HPMC concentration in the films. Also, as the glycerin concentration was reduced, % moisture loss was increased. It is obvious to note that, these hydrophilic excipients tend to hold the moisture and their reduced levels in the films may lead to higher moisture loss **Table 7**.

Percentage Moisture Absorption: The percentage moisture absorption test was carried out to check the physical stability or integrity of the film at the humid condition. The moisture uptake by the films (n=3) was determined by exposing them to an environment of 75% relative humidity (saturated solution of calcium chloride) at room temperature for 1 day. Among all formulations, the formulations containing a higher concentration of HPMC and glycerin showed greater moisture absorption compared to the formulations containing a lower concentration of HPMC **Table 7**. Glycerin and HPMC both being hydrophilic tends to increase the moisture absorption.

Swelling Index: The purpose of measuring swelling index is to determine the ability of hydrophilic polymers used in the formulation to take up water upon hydration. The rate and the extent of film hydration and swelling also affect the drug release from the film. A pre-weighed drug loaded film was placed on a 2% agar plate. An increase in the weight of the film was noted until the constant weight was obtained. The present study revealed that the extent of swelling was directly proportional to the concentration of hydrophilic polymer and hydrophilic plasticizer **Table 7**.

Study of *in-vitro* Disintegration Time of Films: Disintegration time for all the formulations were in a range of 38 ± 2 to 80 ± 1.41 sec. It was observed that as the concentration of polymer increased, the thickness of film increased and thereby time taken for the film to disintegrate increased. The rapid disintegration of MDFs due to an increase in the concentration of plasticizer was due to the rapid uptake of water by the hydrophilic plasticizer, followed by swelling and instantaneous rupture of H-bonds **Table 7**.

TABLE 7: PHYSICAL AND MECHANICAL PROPERTIES OF VARIOUS FILM FORMING POLYMERS

F. code	Tack test	Thickness (mm) ±SD	Weight variation (mg)	Folding endurance	pH	% Moisture loss	% moisture absorption	swelling index	Disintegration time (sec)
F_1	Non-tacky	0.07±0.015	50.40±1.044	100-120	6.1±0.10	10.47± 0.49	8.71±0.25	44%±2.08	51.7±2.94
F_2	Non-tacky	0.08±0.005	54.27±1.593	120-130	6.7±0.20	9.36±0.42	9.56±0.44	47.7%±1.51	45.3±2.65
F_3	Non-tacky	0.09±0.005	58.40±2.449	120-150	6.2±0.26	8.42±0.33	10.83±0.75	50.2%±2.23	38.0±2.00
F_4	Non-tacky	0.11±0.011	60.61±1.417	140-180	6.3±0.10	8.37±0.37	11.60±0.36	60.4%±3.68	59.0±1.00
F_5	Non-tacky	0.11±0.004	65.13±2.080	150-190	6.7±0.11	7.19±0.48	12.68±0.27	69.8%±2.35	55.7±1.63
F_6	Non-tacky	0.13±0.005	69.51±1.445	150-200	7±0.10	6.85±0.71	12.95±0.40	75.2%±3.87	51.6±2.16
F_7	Non-tacky	0.16±0.005	70.22±2.056	200-220	7.6±0.10	6.45±0.46	13.83±0.76	81.1%±2.42	80.0±1.41
F_8	Non-tacky	0.17±0.005	74.51±1.504	210-230	7.5±0.32	4.82±0.26	15.19±0.43	86.3%±4.44	73.7±2.94
F_9	slightly-tacky	0.19±0.005	79.38±1.673	220-250	7.5±0.25	3.69±0.27	15.60±0.35	93.7%±1.41	64.4±2.08

Tensile Strength: By using a TA.XT Plus Texture Analyzer (Texture Technologies, Scarsdale, NY) and miniature tensile grips TA-96B it was observed that as the concentration of the polymer increased,

the tensile strength also increased. The tensile strength of the formulation (F_3) was optimum. F_9 showed the maximum tensile strength and F_1 minimum **Table 8**. This was probably due to the presence of plasticizer that imparts flexibility to the polymer due to the formation of strong hydrogen bonds between the polymer and the plasticizer.

Drug Content Uniformity: The content uniformity test was performed to ensure uniform distribution of the drug. The content uniformity was performed for all the formulations. The results indicated that in all the formulations that there was good uniformity in drug content which ranged between 90.06 to 99.46%. **Table 8** shows the drug content and tensile strength of the formulations.

TABLE 8: DRUG CONTENT AND TENSILE STRENGTH OF FILMS

Formulation code	Drug content	Tensile strength (kg/mm^2)
F_1	95.88±1.18	0.444±0.05
F_2	98.56±1.13	0.457±0.03
F_3	99.46±1.37	0.471±0.06
F_4	97.88±1.18	0.461±0.02
F_5	98.46±1.17	0.510±0.01
F_6	97.40±0.79	0.554±0.04
F_7	97.14±1.61	0.471±0.07
F_8	96.06±0.46	0.567±0.14
F_9	96.88±1.18	0.587±0.09

***In-vitro* Dissolution Study:** The data reveals that the percentage of drug release at the end of 5th min was between 68.8 to 96.8% for formulations F1 to F9. All formulations exhibited essentially similar release pattern, *i.e.*, rapid release during the initial few minutes, followed by a relatively slow release, and finally approaching a plateau level in about 5 min. The rate of release during the early rapid release phase was slightly different in different formulations due to the different concentration of polymer in each formulation. Formulation F3 showed a maximum percentage drug release of 96.8%. This could be attributed to the higher rate and extent of swelling of the larger proportion of the hydrophilic polymer. Formulation F7 showed minimum drug release. This may be due to a higher concentration of polymer but a lower amount of plasticizer (**Table 9**; **Fig. 1**).

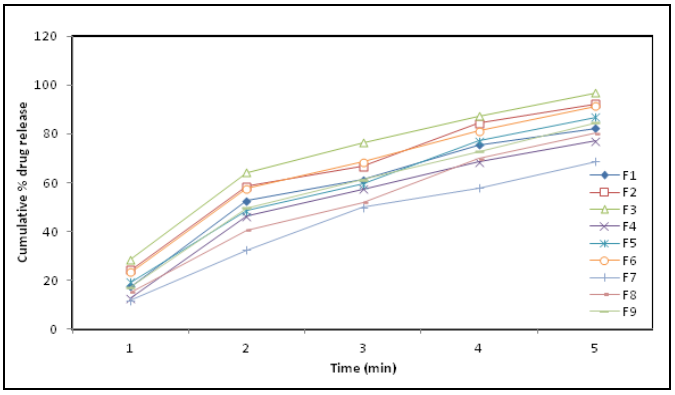

FIG. 1: CUMULATIVE % DRUG RELEASE FROM THE FORMULATIONS F1-F9

TABLE 9: % CUMULATIVE DRUG RELEASE FROM F1 TO F9

Time (sec)	% cumulative drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	17.4	24.2	28.6	12.80	19.30	23.4	11.8	15.2	17.3
2	52.6	58.4	64.2	46.20	48.50	57.6	32.4	40.6	49.7
3	61.2	66.6	76.4	57.30	59.40	68.4	49.8	51.9	61.2
4	75.6	84.4	87.3	68.40	77.20	81.2	57.9	69.8	72.8
5	82.4	92.3	96.8	77.20	86.90	91.3	68.8	80.2	84.6

Surface Morphology Study by SEM: SEM studies were performed to assess the surface morphology of the drug (Losartan potassium) and the prepared films. Losartan potassium showed crystalline structure while MDFs showed smooth surface without any scratches and transverse striations indicating that the drug is uniformly distributed and no crystals of the drug were observed in the prepared films **Fig. 2**.

Accelerated Stability Studies for Optimized Formulation: To determine the change in performance of dosage form on storage, stability study of optimized formulations (F3 and F6) were carried out at 40 ± 2 °C and 75 ± 5% Rh for 2 months. Samples were withdrawn after 10 days interval and evaluated for physicochemical properties. The similarity factor was applied to study the effect of storage on the batch. From the results shown in **Table 10** and **11**, it was concluded that formulations F3 and F6 were stable and retained its original properties with minor differences. There was no physical change in appearance and flexibility. Moreover, there were no major changes in disintegration time and drug content. Hence, the formulations were found to be stable.

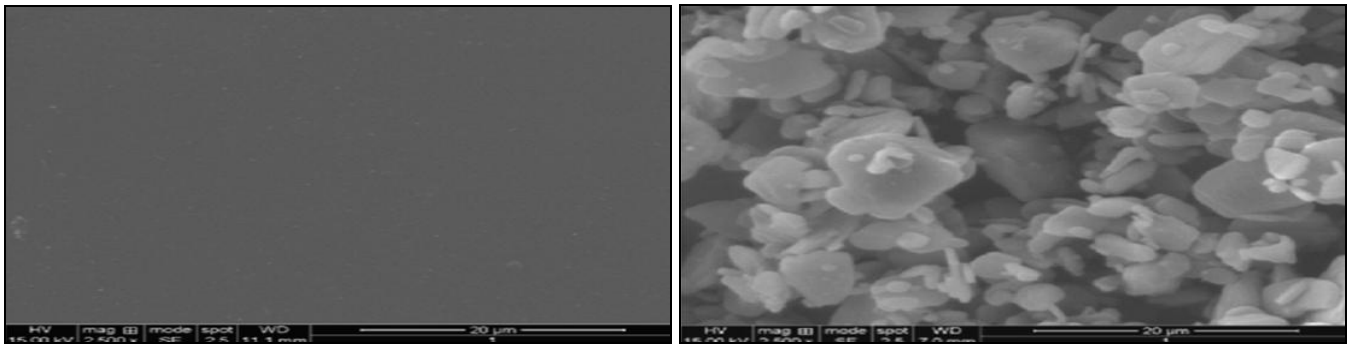

FIG. 2: SEM IMAGES OF A) FILM B) PURE DRUG

TABLE 10: ACCELERATED STABILITY STUDIES OF F3

Parameter	Appearance	Tensile Strength ($kg/mm^{2)}$	Disintegration Time (sec)	Drug content
Initial	Transparent and both surfaces smooth	0.471±0.06	38±2.1	98.59%
After 10 days	Transparent and both surfaces smooth	0.466±0.04	40±1.9	98.27%
After 20 days	Transparent and both surfaces smooth	0.459±0.07	40±1.7	97.95%
After 30 days	Transparent and both surfaces smooth	0.458±0.05	41±2.2	97.63%
After 40 days	Transparent and both surfaces smooth	0.455±0.04	41.8±1.3	97.31%
After 50 days	Transparent and both surfaces smooth	0.445±0.05	42.6±1.9	97.31%
After 60 days	Transparent and both surfaces smooth	0.439±0.08	43.2±1.8	97.31%

TABLE 11: ACCELERATED STABILITY STUDIES OF F6

Parameter	Appearance	Tensile strength ($kg/mm^{2)}$	Disintegration time (sec)	Drug content
Initial	Transparent and both surfaces smooth	0.554±0.04	51.6±2.16	97.40±0.79
After 10 days	Transparent and both surfaces smooth	0.549±0.03	51.8±3.11	97.14±1.19
After 20 days	Transparent and both surfaces smooth	0.542±0.06	52.0±2.21	97.04±0.33
After 30 days	Transparent and both surfaces smooth	0.537±0.05	53.2±1.16	96.96±0.92
After 40 days	Transparent and both surfaces smooth	0.536±0.04	53.7±1.23	96.88±1.85
After 50 days	Transparent and both surfaces smooth	0.536±0.04	54.1±2.14	96.70±0.54
After 60 days	Transparent and both surfaces smooth	0.536±0.04	54.6±1.18	96.18±1.65

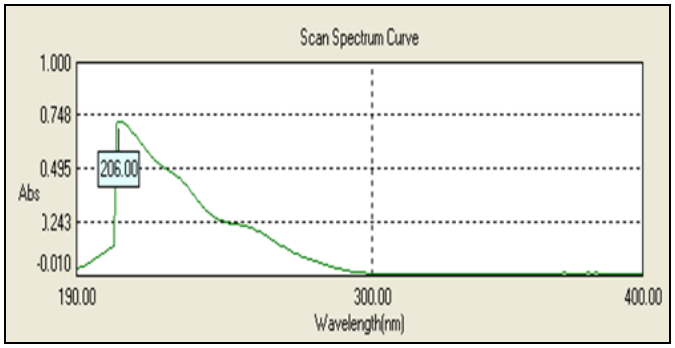

FIG. 3: UV SPECTRUM OF DRUG AND EXCIPIENTS IN PHOSPHATE BUFFER pH 6.8

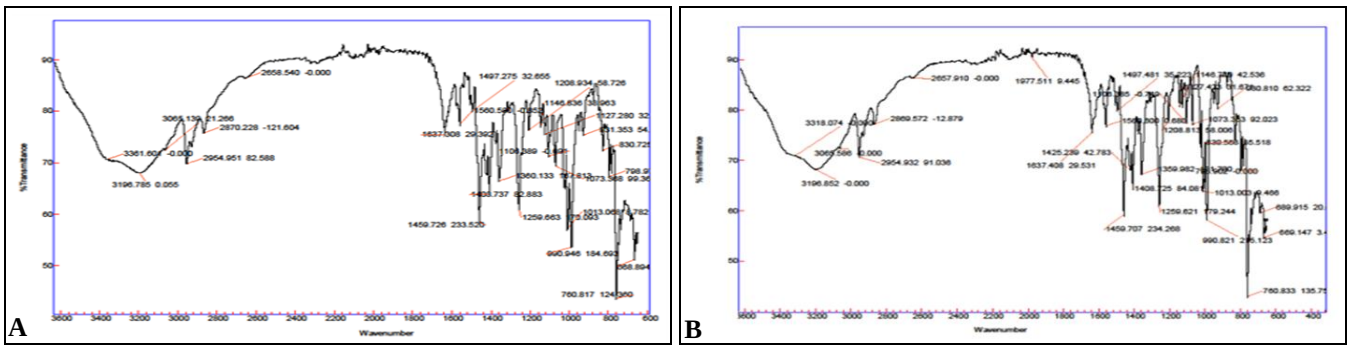

FIG. 4: A) FTIR OF PURE DRUG. B) FTIR OF DRUG AND EXCIPIENTS

Drug - Excipient Interaction Studies: UV and FTIR studies were used to study interaction if any between the drug & excipients. The UV and FTIR scan of a physical mixture of drug and excipients exhibited peaks similar to that of the pure drug, indicating that there was no interaction between the drug and the excipients **Fig. 3** and **4**.

CONCLUSION: The present study revealed that the MDFs of Losartan potassium could be successfully prepared by solvent casting technique with the intention of obtaining better therapeutic efficiency with increasing bioavailability and improving patient compliance. From among the different polymers screened HPMC 5cps showed minimum *in-vitro* disintegration time and maximum tensile strength, compared to other polymers. Hence, it was selected for the preparation of films of the drug. Further, it was concluded that amongst all the different formulations, formulation F_3 and F_6 containing 45% w/w and 50% w/w of polymer concentration respectively were found to be having satisfactory physicochemical and mechanical properties.

Also, the stability study of these two optimized formulations confirmed the longer shelf life of MDFs. Hence, the present study confirms the enormous potential of MDFs for improving patient convenience and compliance, by hastening the onset of action and circumventing hepatic first-pass metabolism, especially in pediatric and geriatric patients.

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