FORMULATION AND EVALUATION OF LOSARTAN POTASSIUM FAST DISSOLVING FILMS USING ALOE VERA GEL

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ABSTRACT

The present study was aimed to develop a novel fast dissolving drug delivery system for an antihypertensive drug. Fast dissolving films (FDF’s) are particularly useful in pediatric, geriatric, psychiatric and bedridden patients who have difficulty in swallowing. Losartan potassium (LP), an antihypertensive drug, is an angiotensin II receptor antagonist. The aim of the present study was to develop FDF’s of LP to increase patient compliance. The FDF’s were prepared by solvent casting method using different grades of low viscosity hydroxypropyl methylcellulose (HPMC) and Aloe vera gel. The FDF’s were evaluated for compatibility, thickness, uniformity of weight, folding endurance, surface morphology, surface pH, moisture uptake, moisture loss, uniformity of drug content, tensile strength, disintegration time and in vitro dissolution studies. DSC and FTIR results indicated that there was no incompatibility between the drug and the polymers. SEM micrograph revealed that the surface morphology of optimized formulation F11 possessed smooth texture and uniform distribution of drug. Moisture uptake was found to be highest (21.79 ± 0.12 %) for Aloe vera containing films suggesting that Aloe vera increases the hydrophilicity and water uptake of the films. The disintegration time was lowest for Aloe vera containing FDF’s and was 16±2.60 sec for formulation F11. In vitro dissolution study showed that the drug release was found to be 98.82±0.33 % at the end of 90mins in 300 ml of pH 6.8 simulated salivary fluid at 37±0.5 °C. The study demonstrated that FDF’s of HPMC E15 with Aloe vera gel could be successfully formulated.

Keywords Aloe vera gel, Losartan potassium, Fast Dissolving Films, HPMC E15, Dysphagia.
I. INTRODUCTION
Fast mouth dissolving films (FDF’s) have become popular as a new delivery system as they are easy to administer and rapid-onset of drug action is possible when the films are placed sublingually. Since the sublingual mucosa is relatively more permeable because of thin membrane lining and is highly perfused, rapid drug absorption and instant bioavailability is possible leading to quick-onset of drug action. Since a major portion of the drug is directly absorbed into the systemic circulation, degradation in the gastrointestinal tract and first pass effect can be avoided. Moreover, better patient compliance can be expected, because this system does not require to be swallowed as is the case of conventional tablets, and therefore is highly beneficial to patients with dysphagia (difficulty in swallowing). The use of mucoadhesive polymers in the films will further enable them to adhere to the sublingual mucosa for longer retention and drug absorption.

Losartan potassium (LP), an antihypertensive drug, is an angiotensin II receptor (type AT) antagonist. It is orally active and undergoes substantial first-pass metabolism by cytochrome P450 enzymes. The terminal half-life of LP is about 2 hrs. The drug is orally administered as 25mg tablets once or twice daily with total daily doses ranging from 25mg to 100mg. Following oral administration, LP is well absorbed and undergoes substantial first-pass metabolism; the systemic bioavailability of Losartan is approximately 33%. Aloe vera has been used for many centuries for its curative and therapeutic properties and although over 75 active ingredients from the inner gel have been identified but therapeutic effects have not been correlated well with each individual component.

In Pharmaceutical industry, it has been used for the manufacture of topical products such as ointments and gel preparations, as well as in the production of tablets and capsules. Important pharmaceutical properties that have recently been discovered for both the Aloe vera gel and whole leaf extract include the ability to improve the bioavailability of co-administered vitamins in human subjects. Due to its absorption enhancing effects, Aloe vera gel has been employed to effectively deliver poorly absorbable drugs through the oral route.

II. MATERIALS AND METHODS
LP was obtained as a gift sample from Killicks Pharma, Mumbai, Maharashtra, India. HPMC E3, E5, E15 LV Premium was obtained from M/S Molychem, Mumbai. PEG 6000 was obtained from Central drug house, New Delhi, India. Aloe gel pure was obtained from...
Pathanjali Ayurved Ltd, Haridwar, India. All other chemicals and solvents used were of analytical grade and were obtained from S.D. Fine-Chem Ltd, Mumbai, India.

**Optimization of components for preparing placebo FDF’s**

The placebo films were prepared from hydroxypropylmethylcellulose (HPMC) E15 LV Premium, which is known for its good film forming capability and acceptability. Hence, HPMC mainly E15 LV Premium grade was evaluated to optimize the effective concentration keeping all other components of the formulations to a constant mean value. Similarly an identical approach was used to optimize the other components such as secondary film forming agents like Aloe gel, HPMC E5 and E3, plasticizer Polyethylene Glycol 6000 using the previously optimized concentration of respective components. The general method of formulating placebo films is as follows. Primary film forming agents and secondary film forming agents were soaked for one hour and uniform stirring was followed for three hours using a magnetic stirrer to obtain a uniform dispersion. Aspartame and plasticizers were dissolved in 95% (v/v) ethanol. Both these aqueous dispersion and alcoholic solutions were mixed to obtain a homogenous dispersion. Finally, this dispersion was casted onto a prefabricated glass mould of size 4x4 cm. This dispersion was dried at 50 °C for 24 hours with an inverted funnel placed over the mould to assist uniform solvent evaporation. The films were carefully removed from the moulds and cut into dimensions of 2x4 cm, packed in aluminum foils and stored in air tight glass containers. The films were evaluated for imperfections and cuts, mechanical strength, thickness, *in vitro* disintegration time and dissolution time.⁹

![Prefabricated glass moulds](image)

**Fig.1 Prefabricated glass moulds**

**Formulation of FDF’s containing LP**

LP loaded FDF’s were fabricated as per the method described for the fabrication of blank FDF’s. LP was incorporated in 95% (v/v) ethanolic solution and the rest of the procedure was same. The compositions of LP loaded FDF’s are shown in Table no. 1
Table 1  Formulation Chart

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Formulations&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F1</td>
</tr>
<tr>
<td>Losartan Potassium (LP)</td>
<td>50</td>
</tr>
<tr>
<td>HPMC E15</td>
<td>200</td>
</tr>
<tr>
<td>HPMC E5</td>
<td>-</td>
</tr>
<tr>
<td>HPMC E3</td>
<td>-</td>
</tr>
<tr>
<td>Aloe vera gel</td>
<td>-</td>
</tr>
<tr>
<td>PEG 6000</td>
<td>40</td>
</tr>
<tr>
<td>Citric Acid</td>
<td>4</td>
</tr>
<tr>
<td>Aspartame</td>
<td>2</td>
</tr>
<tr>
<td>Water (ml)</td>
<td>9</td>
</tr>
<tr>
<td>Ethanol (ml)</td>
<td>1</td>
</tr>
</tbody>
</table>

All the weights are taken in mg, except water and ethanol taken in ml.
<sup>a</sup>Each 4x4 Film contains 50mg of Losartan Potassium.

All the formulations prepared were transparent, flexible and smooth textured except formulation F12 prepared with HPMC E15 and Aloe vera gel in the ratio of 1:3 was unable to peel off from the mould because of stickiness. So Formulation F12 was discarded.

**EVALUATION OF LP LOADED FDF’s**

**Compatibility studies:** The drug-polymer compatibility was confirmed by carrying out FTIR and DSC studies. Drug, polymer and physical mixture of drug-polymer were subjected to FTIR analysis using FTIR 8400S Shimadzu, Japan. Samples were prepared in KBr disks (2 mg sample in 200 mg KBr) with a scan range of 450-4000 cm<sup>-1</sup> and the resolution of 4 cm<sup>-1</sup>. FTIR studies was carried out for LP pure drug, physical mixture of optimized formulation and optimized formulation. DSC analysis using DSC-60 Shimadzu, Japan. Differential scanning calorimetry was performed for pure drug, physical mixture of optimized formulation and optimized formulation. Samples were heated between 30 and 350 °C in an inert nitrogen gas atmosphere at a flow rate of 50 ml/min.

**Film Thickness:** The average weight each of 10 samples of each formulation was determined. The thickness of each of sample was measured using micrometer screw gauge at five different locations, and their mean thicknesses were calculated.
Uniformity of weight: One centimeter square of the film was cut at three different areas from the casted film. The weight of each film was taken and the mean weight was calculated.

Folding Endurance: The FDF (2x4 cm) was repeatedly folded at the same place. The total number of foldings made before the film cracked was denoted as folding endurance value. The FDF was examined for cracks at the area of the bend under a strong light. For each formulation, three samples were examined.

Surface morphology: Surface morphology of LP Film (F11) was performed using scanning electron microscopy (Hitachi S-3700N, Japan) to study the surface texture of films and to determine the uniform distribution of active pharmaceutical ingredient. Samples were mounted on round brass sample holder using double-backed adhesive tapes and then placed in the equipment. Pictures were taken at an excitation voltage of 25 kV.

Drug Content Estimation: The drug content was determined by dissolving one film of dimension 2x4 cm containing 25 mg of LP by homogenization in 20 ml of stimulated saliva of pH 6.8 for 30 min with continuous shaking. Suitably diluted and the absorbance was measured at 254 nm using an UV spectrometer (UV-1800 Shimadzu corporation, Japan). The experiments were carried out in triplicate for the films of all formulations and average values were recorded.

Surface pH: The surface pH of the FDF’s was determined in order to investigate the possible side effects due to change in pH in vivo, since an acidic or alkaline pH may cause irritation to the oral mucosa. The surface pH was determined by using the combined glass electrode (Systronics Handy pH 365, Gujarat, India). The film was allowed to swell by keeping them in contact with 1ml of distilled water (pH 6.5 ± 0.1) for 2 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 tabulated.

Moisture Uptake: The film sample was weighed and placed on a preweighed stainless steel wire mesh. The wire mesh was then submerged in a Petri dish containing 20 ml distilled water. Increase in weight of the film was determined at regular time intervals until a constant weight was obtained. The hydration ratio of the film was calculated using following formula:
\[
PercentHydrationRatio = \frac{W_t - W_0}{W_0} \times 100
\]

Where,
\( W_t \) = Weight of film at time ‘t’
\( W_0 \) = Weight of film at ‘zero’ time.

**Moisture Loss** The percent moisture loss was determined by placing prepared film in desiccators containing anhydrous calcium chloride. After three days, the film was taken and reweighed. The percent moisture loss was calculated using following formula:

\[
PercentMoistureLoss = \frac{W_0 - W_t}{W_0} \times 100
\]

Where,
\( W_0 \) = Initial weight
\( W_t \) = Final weight.

**Tensile Strength:** Tensile strength was determined using Instron 1122 Tensile and Compression Testing machine, India. Film strip of dimension 2x4 cm, free from air bubbles or physical imperfections was held between two clamps positioned at a distance of 3 cm apart. A cardboard was attached on the surface of the clamp via a double sided tape to prevent the film from being cut by the grooves of the clamp. During measurement, the strips were pulled at the bottom clamp by adding weights in pan till the film breaks.

\[
TensileStrength(kg/mm^2) = \frac{Force\ at\ break}{Initial\ crosssectional\ area\ of\ the\ film(mm^2)} \times 100
\]

**In vitro Disintegration time Studies:** The disintegration time is the time when a film starts to break or disintegrate. The *in vitro* disintegration and dissolution time of FDF’s was determined visually in a glass dish of 25 ml simulated salivary fluid with swirling every 10 sec.

**In vitro Dissolution Studies:** *In vitro* dissolution study of FDF’s was studied in USP XIII type-II dissolution apparatus (Electrolab, Model TDT-08L USP, Mumbai, India) employing a paddle stirrer at 100 rpm using 300 ml of pH 6.8 simulated salivary fluid at 37±0.5 °C as dissolution media. A film of 2x4 cm was used in each test. Aliquots of dissolution medium (5 ml) was withdrawn at predetermined time intervals and analyzed for drug content by measuring the absorbance at 254 nm. The volume withdrawn at each interval was replaced.
with fresh quantity of dissolution medium. Cumulative percentage of drug released was calculated and plotted against time.

**Stability Studies**

Stability tests are the series of tests designed to obtain information on the stability of the pharmaceutical product in order to define its shelf life and utilization period under specified packaging and storage conditions.

From the eleven formulations, optimized formulation was tested for stability studies. FDF’s of optimized formulation were stored at two different storage conditions namely 30 ± 0.5 °C/60 ± 1% RH and 40 ± 0.5 °C/75 ± 1% RH. Each film was wrapped in a butter paper followed by aluminum foil and placed in an aluminum pouch, which was heat-sealed at the end. The films were evaluated for drug content, surface pH, moisture uptake, disintegration time, *in vitro* drug release after storage for 90 days. The values for *in vitro* drug release from the films were calculated and were compared for change in the dissolution profile.

**III. RESULTS AND DISCUSSION**

**Fourier Transform Infrared (FTIR) Spectroscopy**

![FTIR Spectra of pure drug Losartan Potassium](image)

Fig 2 FTIR spectra of pure drug Losartan Potassium
FTIR studies was carried out for the pure drug – Losartan potassium, formulation F11 and their spectra are as shown in fig 2 & fig 3 respectively.

The characteristic peaks of the pure drug – Losartan Potassium was assigned from standard literature. These included N-H stretching, C-H stretching, C=N stretching and are as shown below.

1. 3566.50 cm⁻¹: O-H stretching
2. 3383.26 cm⁻¹: N-H stretching
3. 2956.97 cm⁻¹: C-H stretching
4. 1423.51 cm⁻¹: C-H bending
As seen in fig 2, the spectra for LP exhibits a broad peak at 3566.50 cm\(^{-1}\) due to alcohols and phenols (O-H) stretching vibration, 3383.26 cm\(^{-1}\) due to primary and secondary amine (N-H) stretching vibration and 2956.97 cm\(^{-1}\) due to alkanes (C-H) stretching vibration.

The FTIR results from formulation F11 exhibited broad peaks at 3435.34 cm\(^{-1}\) due to alcohols and phenols (O-H) stretching vibration, 3397.40 cm\(^{-1}\) due to primary and secondary amine (N-H) stretching vibration, 2931.90 cm\(^{-1}\) due to alkanes (C-H) stretching vibration.

The intensity and position of these characteristic peaks permits easy interpretation of any possible interaction between the drug and the excipients in the formulation. The results clearly showed that there was no interaction between the drug and the excipients in the prepared formulation F11. The drug - Losartan Potassium was intact and there was no sign of any degradation due to preparative processes adopted during the loading of the drug into oral fast dissolving films.

Differential Scanning Calorimetry (DSC)

![DSC thermogram of pure drug Losartan Potassium](image)
Thermal characterization and analysis of DSC curves of the pure drug, physical mixture of Formulation F11 was carried out. The studies provided thermal behavior of the pure drug, its physical mixture with HPMC E15, Aloe vera gel, PEG 6000, Aspartame, Citric acid. Losartan Potassium showed an endothermic peak at 169.8 °C and an exothermic peak at 271.5 °C. Physical mixture of Formulation F11 showed an endothermic peak at 55 °C, 170 °C and exothermic peaks at 62 °C and 249 °C.

The above results indicated that the characteristic peaks of LP appeared in the physical mixture of Formulation F11 indicating that there was no possible interaction between the drug and the excipients in the FDF formulation. The drug in all probability was present in its stable form without any possible degradation.

Thickness
The Thickness of the formulated films was found to be in a range of 0.13 ± 0.01 mm to 0.8 ± 0.02 mm. The mean values are tabulated in Table 2. Obtained results showed that with increase in film thickness, disintegration time increased. Further increase in thickness of film increased the crystallinity of film and decreased dissolution rate.

Uniformity of weight
LP loaded FDF’s (1x1 cm) was tested for uniformity of weight and the results are tabulated in table no.2. The percentage deviation weight of the films varied from 0.09 % to 0.67 %.
According to Indian Pharmacopoeia for dosage form with less than 100 mg drug content, 10% deviation was allowed. All the formulations were found to be within the acceptable limits. LP is a potent drug and weight uniformity of the dosage form is a very important parameter to be considered. In the present study all the formulations were found to be within the acceptable range of percentage deviation of the weight and could be used for the further evaluation.

**Folding Endurance**

Folding endurance measures the ability of patch to withstand rupture. Higher the folding endurance lower will be the chances of film to rupture easily and vice versa. All Formulations were having good folding endurance values ranging from $260 \pm 0.09$ to $482 \pm 0.013$ except for formulation F3 which had a low folding endurance value of $53 \pm 0.21$ and thickness of about 0.8 mm. The folding endurance of all the formulations was tabulated in Table 2. Increase in concentration of HPMC E15 in the formulations decreased folding endurance, which was due to increase in thickness of the film. Higher the thickness of the films lower was the folding endurance values. The results implies that the prepared formulations are suitable for large scale manufacturing to produce long continuous films without breaking during casting processing, package and transportation.

**Surface morphology**

SEM studies was carried out for optimized formulation F11 (Fig 7) using Hitachi S-3700N scanning electron microscopy, Japan. SEM micrograph revealed that the surface morphology of formulation F11 possessed smooth texture and uniform distribution of drug.

![Fig 7 SEM Micrograph of formulation F11.](image)
Content uniformity
The content uniformity test was performed to ensure uniform distribution of drug. The content uniformity was performed for all the formulations and was tabulated in table no. 2. Obtained results indicate that in all the formulations drug content was uniform and ranged between 95.61 % to 97.19 %. The cumulative percent drug released by each film in the in vitro release studies was based on the mean content of drug present in the respective film.

Surface pH
Surface pH evaluation of FDF’s is an important characterization study. An acidic or alkaline pH may cause mucosal irritation. All the formulations were within the salivary pH range (Table 2) and were suitable for oral application owing to the acceptable pH measurements.\(^\text{15}\)

Moisture uptake
Moisture absorption study is an important parameter to be determined, as the presence of moisture poses a critical challenge on drug stability. All the reported values are as shown in the Table No.2. It was observed that all the polymers HPMC E15, E5, E3 and Aloe vera gel were hydrophilic in nature and the moisture uptake values ranged from 4.32 ± 0.09 % to 21.79 ± 0.12 %. Moisture uptake is inversely proportional to disintegration time. Optimized formulation F11 containing 1:1 ratio of HPMC E15 (100 mg) and Aloe vera gel (100 mg) possessed a highest percent hydration ratio 21.79 ± 0.12 with the least disintegration time of 16 sec. High water absorption capacity can be attributed to Aloe vera which imparts and enhances the hydrophilic properties of FDF’s.

Moisture loss
The moisture loss study gives an idea about nature, stability and ability of films to retain its physicochemical properties under normal storage conditions. It also gives an idea about hydrophilicity of films. All the obtained values are reported in Table No.2. The obtained values are almost uniform and ranged from 0.28 ± 0.06 % to 1.21 ± 0.04 % indicating low moisture uptake and stable formulations.

Tensile Strength: Tensile strength of all formulations was found to be in a range of 2.96 ± 0.09 to 5.98 ± 0.05 kg/cm\(^2\). It was observed that with increase in thickness of film, there was a decrease in tensile strength and increase in disintegration time. There is no much difference between the tensile strengths of all formulations except for formulation F2 and F3 which had higher thickness compared to all other formulations. All the formulations had uniform tensile strength values except for Formulation F2 & F3 which were thicker than the rest.
Table 2: Evaluation of Fast Dissolving Films

<table>
<thead>
<tr>
<th>Properties</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
<th>F10</th>
<th>F11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thickness(^a) (mm)</td>
<td>0.30±0.01</td>
<td>0.50±0.01</td>
<td>0.80±0.02</td>
<td>0.30±0.01</td>
<td>0.25±0.01</td>
<td>0.25±0.02</td>
<td>0.25±0.01</td>
<td>0.20±0.01</td>
<td>0.15±0.01</td>
<td>0.13±0.01</td>
<td></td>
</tr>
<tr>
<td>Mean weight(^a) (1x1 cm film) (mg)</td>
<td>53.74±0.43</td>
<td>118.89±0.12</td>
<td>153.50±0.53</td>
<td>53.68±0.33</td>
<td>61.22±0.14</td>
<td>54.22±0.67</td>
<td>54.13±0.11</td>
<td>61.64±0.09</td>
<td>53.07±0.46</td>
<td>54.36±0.22</td>
<td>33.77±0.26</td>
</tr>
<tr>
<td>Drug Content(^a) (%)</td>
<td>96.51±0.05</td>
<td>95.95±0.07</td>
<td>96.51±0.26</td>
<td>96.18±0.13</td>
<td>95.95±0.07</td>
<td>96.51±0.10</td>
<td>96.96±0.04</td>
<td>96.85±0.06</td>
<td>96.40±0.12</td>
<td>96.96±0.09</td>
<td>97.19±0.05</td>
</tr>
<tr>
<td>Surface pH(^a)</td>
<td>7.40±0.60</td>
<td>7.40±0.50</td>
<td>7.30±0.60</td>
<td>7.20±0.40</td>
<td>7.30±0.60</td>
<td>7.20±0.70</td>
<td>7.50±0.50</td>
<td>7.40±0.60</td>
<td>7.20±0.50</td>
<td>7.20±0.50</td>
<td>7.30±0.40</td>
</tr>
<tr>
<td>% Hydration ratio(^a)</td>
<td>8.32±0.06</td>
<td>6.74±0.21</td>
<td>4.32±0.09</td>
<td>9.91±0.06</td>
<td>12.87±0.03</td>
<td>17.61±0.03</td>
<td>10.53±0.01</td>
<td>17.58±0.10</td>
<td>19.57±0.08</td>
<td>21.03±0.09</td>
<td>21.79±0.12</td>
</tr>
<tr>
<td>% Moisture Loss(^a)</td>
<td>0.90±0.02</td>
<td>0.33±0.01</td>
<td>0.28±0.06</td>
<td>0.74±0.03</td>
<td>0.75±0.02</td>
<td>0.80±0.03</td>
<td>0.96±0.01</td>
<td>0.88±0.02</td>
<td>0.88±0.01</td>
<td>0.80±0.04</td>
<td>1.21±0.04</td>
</tr>
<tr>
<td>Tensile strength(^a) (kg/cm(^2))</td>
<td>5.26±0.04</td>
<td>3.82±0.02</td>
<td>2.96±0.09</td>
<td>5.34±0.04</td>
<td>5.26±0.07</td>
<td>5.34±0.02</td>
<td>5.34±0.08</td>
<td>5.29±0.01</td>
<td>5.45±0.02</td>
<td>5.73±0.06</td>
<td>5.98±0.05</td>
</tr>
<tr>
<td>Folding endurance(^a) (sec)</td>
<td>380±0.12</td>
<td>260±0.09</td>
<td>53±0.21</td>
<td>352±0.01</td>
<td>423±0.03</td>
<td>446±0.11</td>
<td>298±0.04</td>
<td>429±0.05</td>
<td>449±0.07</td>
<td>426±0.01</td>
<td>482±0.01</td>
</tr>
<tr>
<td>Disintegration time(^a) (sec)</td>
<td>184±1.00</td>
<td>426±1.30</td>
<td>615±1.90</td>
<td>140±1.00</td>
<td>123±2.20</td>
<td>98±1.80</td>
<td>126±2.10</td>
<td>99±1.50</td>
<td>88±1.00</td>
<td>22±3.00</td>
<td>16±2.60</td>
</tr>
<tr>
<td>% Cumulative drug release (90 min)</td>
<td>93.32±0.37</td>
<td>89.62±0.42</td>
<td>84.55±0.29</td>
<td>94.40±0.46</td>
<td>95.92±0.35</td>
<td>96.48±0.87</td>
<td>95.92±0.66</td>
<td>96.62±0.40</td>
<td>96.86±0.55</td>
<td>98.41±0.52</td>
<td>98.82±0.33</td>
</tr>
</tbody>
</table>

\(^a\)Mean ± SD; n = 3
In vitro Disintegration time Studies
The disintegration time is the time when a film starts to break or disintegrate. Disintegration time for all the formulated films are tabulated in Table 2. Disintegration time for all the formulations were in a range of 16 ± 2.6 sec to 615 ± 1.9 sec. It was observed that as the concentration of polymer increased, thickness of film increased and thereby time taken for the film to disintegrate increased. Formulation F11 a combination of Aloe vera gel and HPMC E15 in the ratio of 1:1 showed least disintegration time of 16 ± 2.6 sec compared to all other formulations because of its ability to rapidly dissolve in water. The rapid disintegration of FDF’s was due to the rapid uptake of water by the of hydrophilic polymers (HPMC E15, E5, E3 & Aloe vera gel), followed by swelling and instantaneous rupture of H-bonds.

In vitro Dissolution Studies

![Graph showing in vitro drug release profiles of formulations F1 – F11](image)

**Fig.8 In vitro drug release profiles of formulations F1 – F11**

In vitro dissolution studies were carried in simulated salivary fluid of pH 6.8. The data reveals that the percentage drug release at the end of 90th minute was between 84.55% to 98.82% for formulations F1 to F11. The dissolution profiles of all the formulations are depicted in fig 8. Optimized formulation F11, containing HPMC E15 and Aloe vera gel in the ratio of 1:1 released 98.82% drug at the end of 90th minute. Rapid dissolution of FDF’s was due to the hydrophilic nature of the polymers used in film formation and PEG 6000 which was used as the plasticizer. When HPMC E15 and Aloe vera containing films were exposed to water, HPMC facilitated rapid water absorption followed by rapid disintegration and dissolution of the drug. PEG 6000 promoted wetting and improved solubility due to the PEG rich micro environment resulting in faster dissolution rates. It may be noted a combined
effect of wetting, high degree of water uptake and co-solvent effects may be contributing factors for rapid dissolution of FDF’s.

Stability studies
Formulation F11 was selected for stability studies on the basis of low disintegration time and high cumulative % drug release. From these results it was concluded that, formulation F11 is stable and retained their original properties with minor differences. The in vitro release profile of F11 at 30 ± 0.5 °C/60 ± 1% RH and 40 ± 0.5 °C/75 ± 1% RH conditions after 90 days was 98.06% and 96.15%, respectively, has indicated that no or minor alteration after storage.

V. CONCLUSION
Fast Dissolving Films of Losartan Potassium was prepared using low viscosity film formers like HPMC E15 in combination with HPMC E5, E3, Aloe vera gel and polyethylene glycol 6000 as a plasticizer by solvent casting method. The films were smooth textured with good surface morphology and possessed adequate mechanical strength. Losartan Potassium could be successfully incorporated uniformly and rapid disintegration & dissolution could be achieved with little or no water. From the study it can be concluded that HPMC along with Aloe vera gel could be successfully formulated into fast dissolving film for immediate release without the need of superdisintegrants.

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VII. REFERENCES


