ABSTRACT
Fast dissolving films have been played an important role in the current pharmaceutical research. They have convenience and ease of use over other dosage forms such as orally disintegrating tablets and immediate release tablets. In the present research, rapidly dissolving films of loratidine were developed using low viscosity grades of HPMC as film forming polymers. HPMC is a water soluble synthetic polymer which was used as film former form many years. The films of loratidine were prepared by solvent casting method using di-chloromethane and methanol as solvents. The prepared films were evaluated for drug content, weight variation, thickness and in vitro in vivo disintegration time. Loratidine is moderately bitter drug; taste masking was achieved by use of sweeteners, flavours and citric acid. Type of flavor significantly affected the taste masking property. The in vitro and in vivo disintegration time of the optimized formulation was found to be below 29 seconds and 24 seconds respectively. The prepared films exhibited good integrity and thickness. In vitro dissolution studies were performed as per the FDA dissolution guidelines for about 10 minutes, the optimum formulation released complete drug within 4-6 minutes. FTIR studies showed no drug polymer interaction.

KEY WORDS: loratidine, fast dissolving, films, solvent casting, disintegration.

INTRODUCTION
Oral route is the most preferred route for the delivery of the drugs till date as it bears various advantages over the other route of drug administration, but oral drug delivery systems still need some advancements to be made because of their some drawbacks related to particular class of patients which includes geriatric, pediatric and dysphasic patients associated with many medical conditions as they have difficulty in swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take solid preparations due to
fear of choking. Even with fast dissolving tablets there is a fear of choking due to its tablet type appearance. One study showed that 26% of 1576 patients experienced difficulty in swallowing tablets. The most common complaint was tablet size, followed by surface form and taste. The problem of swallowing tablets was more evident in geriatric and pediatric patients, as well as travelling patients who may not have ready access to water [1-4]. So, fast-dissolving drug-delivery systems came into existence in the late 1970’s as an alternative to tablets, capsules and syrups for pediatric and geriatric patients who experience difficulties in swallowing traditional oral solid-dosage forms. These systems consist of the solid dosage forms that disintegrate and dissolve quickly in the oral cavity without the administration of water. Research and development in the oral drug delivery segment has led to transition of dosage forms from simple conventional tablets or capsules to modified release tablets or capsules to oral disintegrating tablet (ODT) to wafer to the recent development of oral fast dissolving films (OFDFs). Amongst the plethora of avenues explored for the rapid drug releasing products, oral strip technology is gaining much attention [5, 6].

Orally fast-dissolving film is new drug delivery system for the oral delivery of the drugs. It was developed on the basis of technology of the transdermal patch. The delivery system consists of a very thin oral strip, which is simply placed on the patient’s tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates and dissolves to release the medication for oromucosal and intra gastric absorption. Technology Catalysts forecasts the market for drug products in oral thin film formulations was valued of $500 million in 2007 and could reach $2 billion in 2012. Based on upward global growth trends of the past decade, the fast dissolving dosage market could produce revenues of $13 billion by 2015[7, 8].

**Special features of mouth dissolving films**

- Thin elegant film
- Available in various size and shapes
- Unobstructive
- Excellent mucoadhesion
- Fast disintegration
- Rapid release
The ideal characteristics of a drug to be selected

- The drug should have pleasant taste.
- The drug to be incorporated should have low dose upto 40 mg.
- The drugs with smaller and moderate molecular weight are preferable.
- The drug should have good stability and solubility in water as well as in saliva.
- It should be partially unionized at the pH of oral cavity.
- It should have the ability to permeate oral mucosal tissue.

Advantage of orally fast dissolving films

- Oral dissolving films can be administered without water, anywhere, any time.
- Due to the presence of larger surface area, films provide rapid disintegrating and dissolution in the oral cavity.
- Oral dissolving films are flexible and portable in nature so they provide ease in transportation, during consumer handling and storage.

MATERIALS AND METHODS

Materials

Hpmc 5 cps, dichloromethane, ethanol, Hpc, ethyl cellulose, glycerin, tween -80, aspartame.

Method

Formulation Of Fast Dissolving Film

In the present study, fast dissolving films of loratidine were prepared by solvent casting technique. Flat, square-shaped, glass moulds having a surface area of 42.25 cm² were fabricated for casting the films.

Preparation of casting solutions

The casting solutions were prepared by dissolving weighed quantities of polymers in 10 ml of solvent mixture taken in a beaker. The drug and aspartame were dissolved in 5 ml of solvent mixture and added to the above polymer solution along with glycerol, as plasticizer, thoroughly mixed to form a homogeneous mixture. The volume was made up to 20 ml with solvent mixture. The beaker was covered with aluminium foil and the solution was allowed to stand overnight to remove air bubbles.
Preparation of fast dissolving films

The casting solution (20 ml) was poured into glass moulds and kept a side covered with funnel to allow for controlled evaporation. The films were removed by peeling and cut into square dimension of 2 x 2 cm (4 cm²), so that each film contained about 10 mg of drug. These films were kept in desiccator for 2 days for further drying and wrapped in aluminium foil, and packed in self-sealing covers.

Formulation

Table 1: formulation of oral dissolving films

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F1</td>
</tr>
<tr>
<td>Loratidine (mg)</td>
<td>115</td>
</tr>
<tr>
<td>HPC (mg)</td>
<td>230</td>
</tr>
<tr>
<td>HPMC 5cps (mg)</td>
<td>---</td>
</tr>
<tr>
<td>EC (mg)</td>
<td>---</td>
</tr>
<tr>
<td>Glycerine (mg)</td>
<td>80</td>
</tr>
<tr>
<td>Tween-80 (mg)</td>
<td>60</td>
</tr>
<tr>
<td>Aspartame (mg)</td>
<td>15</td>
</tr>
<tr>
<td>Ethanol (ml)</td>
<td>16</td>
</tr>
<tr>
<td>Dichloro methane (ml)</td>
<td>4</td>
</tr>
<tr>
<td>Mint flavour</td>
<td>q.s</td>
</tr>
</tbody>
</table>

Determination of λmax

A 100 mg of Loratidine was accurately weighed and was dissolved in 100 ml pH 7.4 buffer solution. Take the one ml solution then diluted with pH 7.4 buffer solution to 10 ml. again collect the one ml solution from the 10 ml and diluted to 10 ml with pH 7.4 buffer solution. Finally UV spectrum was recorded in the wavelength range 200-400 nm.

II. Preparation of calibration curve for Loratidine

A standard curve was prepared by dissolving 100 mg of Loratidine in 100 ml pH 7.4 buffer solution. It was further diluted with pH 7.4 buffer solution to get solutions in concentration range of 10μg/ml to 50μg/ml. The absorbance of these solutions was determined spectrophotometrically at 247 nm.

Evaluations of Fast dissolving film:[9]

Film Thickness

The thickness of 3 films of each formulation was performed by screw gauge at different position of the film and the average thickness was calculated.
Uniformity of weight
The film (4 cm²) was cut at five different places in the cast film. The weight of each filmstrip was taken and the weight variation was calculated.

Uniformity of drug content
This parameter was determined by dissolving one film of dimension 2 × 2 cm containing 10 mg of loratidine by homogenization in a mixture of 5 ml of ethyl alcohol and 100 ml of simulated saliva of pH 6.75 for 30 min with continuous shaking. Then the solution was filtered and after suitable dilution with simulated salivary fluid, the absorbance was measured at 247 nm using a UV spectrophotometer and the drug content was calculated.

Folding endurance
The folding endurance is expressed as the number of folds (number of times the film is folded at the same place) required to break the specimen or to develop visible cracks. This also gives an indication of brittleness of the film. A strip of 2 × 2 cm (4 cm²) was subjected to folding endurance by folding the film at the same place repeatedly several times until a visible crack was observed, and the values were reported.

Surface pH
The film to be tested was placed in a Petri dish and was moistened with 0.5 ml of distilled water and kept for 30 s. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and allowing equilibration for 1 min. the average of three determinations for each formulation was done.

Tensile Strength
The tensile strength was determined by the apparatus designed as shown in fig.1. The instrument was designed such that it had horizontal wooden platform with fixed scale and attachments for two clips that holds films under test. Out of the two clips one was fixed and other was movable. Weights were hanged to one end of pulley and the other end of pulley was attached with movable clip. The wooden platform was such fitted that it would not dislocate while the test is running. Three strips of films were cut having 2 cm length and 2 cm breadth. The thickness and breadth of strips were noted at three sites and average value was taken for calculation.
The rate of change of stress was kept constant with the increment of 0.5g per 2 minutes. The elongation was observed and the total weights taken were used for calculation. The tensile strength was calculated by using following formula.

\[
Tensile\ stress(S) = \frac{Applied\ force}{Cross\ sectional\ area} = \frac{mg}{bt}
\]

Where, \( S \) = tensile stress in 980 dynes/cm\(^2\)
\( m \) = mass in grams
\( g \) = acceleration due to gravity (980 dynes/cm\(^2\))
\( b \) = breadth of strip in centimeters
\( t \) = thickness of strip in centimeters

The strain is change resulting in size of strip after the force was applied to its original size. Therefore, the strain can be given as,

\[
Strain(E) = \frac{Total\ elongation}{Original\ length} = \frac{L - L_0}{L_0}
\]

Where, \( L \) = length after force was applied
\( L_0 \) = original length

**Percent elongation**

The percent elongation at break was measured by formula given below.

\[
Strain(E) = \frac{Total\ elongation}{Original\ length} \times 100 = \frac{L - L_0}{L_0} \times 100
\]

Where, \( L \) = length after force was applied
\( L_0 \) = original length
Disintegration test
Disintegration test was performed to ensure the disintegration of the film in water. One film from each formulation was introduced into one tube of disintegration apparatus IP. A disc was added into the tube. The assembly was suspended in a beaker containing simulated saliva and the apparatus was operated until the film disintegrated. Test was performed in triplicate.

In vitro dissolution studies
The simulated salivary fluid containing 2% ethanol after considering solubility factors of the drug was taken as the dissolution medium to determine the drug release. The dissolution profile of quick release films of loratidine was carried out using USP type II (paddle apparatus) with 300 ml of simulated salivary fluid (pH 6.8) as dissolution medium maintained at 37± 0.5°C. The medium was stirred at 100 rpm. Aliquots (5 ml) of the dissolution medium were withdrawn at every 30 sec time interval and replacing the same amount with the fresh medium. Amount of drug in the withdrawn samples was determined by UV spectrophotometer at 247 nm. Three trials were carried out for all the samples and the average value was taken. The percentage of drug dissolved at various time intervals was calculated and plotted against time.

In vitro disintegration studies
Disintegration time gives an indication about the disintegration characteristics and dissolution Characteristics of the film. The film as per the dimensions (2 x 2 cm) required for dose delivery was placed on a stainless steel wire mesh placed in a petridish containing 10 ml 0.1N Hcl. Time required for the film to break was noted.

RESULTS AND DISCUSSION
Five formulations of Loratidine fast dissolving films were formulated using different polymers. The prepared films were subjected to evaluation parameters like thickness, drug content, folding endurance, tensile strength h, % elongation, In vitro drug release studies etc.

A. Preformulation studies
a. Melting point determination:
The melting points were found to be in the range of 134-137°C.
b. Calibration curve of Loratidine:
The absorbance values obtained are shown in table. Using concentration and absorbance data, Beer and Lambert’s plot was obtained.
Table 2: calibration curve of loratidine in PH 7.4 buffer

<table>
<thead>
<tr>
<th>Concentration(µg/ml)</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>0.148</td>
</tr>
<tr>
<td>20</td>
<td>0.267</td>
</tr>
<tr>
<td>30</td>
<td>0.394</td>
</tr>
<tr>
<td>40</td>
<td>0.531</td>
</tr>
<tr>
<td>50</td>
<td>0.674</td>
</tr>
</tbody>
</table>

Figure 2 : calibration curve of loratidine in PH 7.4 buffer

[B. Physical evaluation

1. Thickness: The thickness of the films in each set was measured. The marginal difference in the thickness was observed among each group indicated that more the amount of polymer, higher the thickness values. The individual weight of samples of each type formulation was determined and the average weight was calculated. It was observed that weight of the entire film sample in each formulation was uniform. No significant difference in the drug content among the films, indicated good content uniformity.

2. Tensile strength & % elongation: The tensile strength gives an indication of the strength and elasticity of the film reflected by the parameters, tensile strength (TS) and elongation at break (E/B). The results showed that, among the formulations F1 and F5, the tensile strength and % elongation increased with the increase in the percentage of mucoadhesive polymer, HPMC. Tensile strength and % elongation of the films was recorded in the Table.

3. Folding Endurance: All the films showed good folding endurance greater than 300, indicated that the films have good flexibility.
4. **Weight variation:** It was observed that weight of the entire film sample in each formulation was uniform. No significant difference in the drug content among the films, indicated good content uniformity.

5. **Surface pH:** The surface pH was found to be in the range of 6.2 to 7.06, which is close to neutral pH, which indicated that films may have less potential to irritate the sublingual mucosa, thereby they are comfortable.

6. **Disintegration time:** The disintegration time of the film was done by using disintegration test apparatus. The formulation F4 shows 40 sec disintegration time. Disintegration time of the films was found to be decreased with increase in the concentration of the HPMC polymer (Table). When placed over the tongue, the film dissolved instantly. Dissolution was also found to be improved due to salivary stimulation in the presence of the sweetener (aspartame).

7. **Drug content:** Total drug content per film was estimated by taking Film of 2×2cm² was cut and placed in 50 ml volumetric flask and dissolved in buffer (7.4 pH). Than 1 ml solution was pipette out and diluted to 10 ml with buffer (7.4 pH). The absorbance of the solution was measured at 242 nm. The drug content was in the range of 92.40 to 98.9 %. The values are given in the table no.3.

**Table 3: percentage of drug content**

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Drug content (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>92.40</td>
</tr>
<tr>
<td>F2</td>
<td>97.1</td>
</tr>
<tr>
<td>F3</td>
<td>94</td>
</tr>
<tr>
<td>F4</td>
<td>98.9</td>
</tr>
<tr>
<td>F5</td>
<td>97.5</td>
</tr>
</tbody>
</table>

**Table 4: Physicochemical evaluation data of Loratidine fast dissolving film.**

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Appearance</th>
<th>Weight (mg)</th>
<th>Thickness (mm)</th>
<th>Tensile strength (kg/cm²)</th>
<th>% Elongation</th>
<th>Surface pH</th>
<th>Folding Endurance</th>
<th>D.T (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>Opaque</td>
<td>47.67</td>
<td>0.08</td>
<td>0.623 ±0.020</td>
<td>28.93 ±0.450</td>
<td>6.41</td>
<td>&gt;300</td>
<td>59</td>
</tr>
<tr>
<td>F2</td>
<td>Opaque</td>
<td>49.51</td>
<td>0.09</td>
<td>0.503 ±0.025</td>
<td>25.73 ±0.416</td>
<td>6.48</td>
<td>&gt;300</td>
<td>57</td>
</tr>
<tr>
<td>F3</td>
<td>Opaque</td>
<td>48.78</td>
<td>0.11</td>
<td>0.366 ±0.015</td>
<td>20.93 ±0.585</td>
<td>6.59</td>
<td>&gt;300</td>
<td>51</td>
</tr>
<tr>
<td>F4</td>
<td>Transparent</td>
<td>46.82</td>
<td>0.12</td>
<td>1.223</td>
<td>64.16</td>
<td>7.04</td>
<td>&gt;300</td>
<td>40</td>
</tr>
</tbody>
</table>
In vitro drug release studies

Table 5: In vitro Dissolution Profile comparison of formulations F1, F2, F3, F4, F5

<table>
<thead>
<tr>
<th>TIME (Min)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>40.12</td>
<td>23.45</td>
<td>46.12</td>
<td>41.56</td>
<td>37.56</td>
</tr>
<tr>
<td>4</td>
<td>55.24</td>
<td>46.29</td>
<td>62.59</td>
<td>55.68</td>
<td>45.67</td>
</tr>
<tr>
<td>6</td>
<td>67.25</td>
<td>55.67</td>
<td>61.59</td>
<td>69.84</td>
<td>56.39</td>
</tr>
<tr>
<td>8</td>
<td>82.16</td>
<td>69.78</td>
<td>77.89</td>
<td>81.27</td>
<td>68.73</td>
</tr>
<tr>
<td>10</td>
<td>92.5</td>
<td>81.39</td>
<td>88.36</td>
<td>98.49</td>
<td>84.65</td>
</tr>
</tbody>
</table>

Films prepared with different polymer concentration with all formulations drug release profiles as shown in table in that first three formulations are very thin (0.08-0.11 mm) and tensile strength (0.623 -0.366 Kg/cm²). Formulation (F4) showed better tensile strength with satisfactory D.T. (40 sec) in comparison to other formulations (F1, F2, F3 and F5). Addition of plasticizer has shown significance difference in folding endurance and tensile strength. The prepared film containing Loratidine was clear and colorless in F4 & F5. The drug release from F5 is less, so F4 was good formulation among all formulations.

Compatibility studies

Compatibility studies were performed using FT-IR spectrophotometer. The FT-IR spectrum of pure drug and physical mixture of drug and polymers were studied. The interpretation results were summarized in table no (8)
Table 6: FT-IR Interpretation

<table>
<thead>
<tr>
<th>S No</th>
<th>Wave number(cm⁻¹)</th>
<th>Type of stretch</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3435.34</td>
<td>0-H</td>
</tr>
<tr>
<td>2</td>
<td>1643.41</td>
<td>C=C</td>
</tr>
<tr>
<td>3</td>
<td>1446.66</td>
<td>CH₃</td>
</tr>
<tr>
<td>4</td>
<td>1705.13</td>
<td>C=0 (Aromatic Aldehyde)</td>
</tr>
<tr>
<td>5</td>
<td>1643.41</td>
<td>C=0 (Aromatic Acid)</td>
</tr>
</tbody>
</table>

**Figure 4: Ftir Of Pure Drug**

**Figure 5: Ftir Of Drug And Polymer**

**Figure 6: Ftir Of Optimized Formulation**
SUMMARY & CONCLUSION

The main objective of the study was to formulate and evaluate fast dissolving film containing Loratidine. The fast dissolving films can be easily formulated by solvent casting method by using polymers such as HPMC, HPC and EC in different ratios with suitable plasticizer like glycerin and Tween-80 and sweetener like aspartame. It was observed that the physicochemical characteristics such as uniformity of weight, thickness, folding endurance, surface pH, and uniformity of drug content of all the film samples showed satisfactory results with respect to variation of these parameters between films of same formulation. Based on the physicochemical parameters and in vitro drug release studies, formulation F4 considered as the best formulation which exhibited the drug release of 98.49%. At the end of 10 min. Present study reveals that all the five formulated films showed satisfactory film parameters. From the present investigation it can be conclude that fast dissolving film formulation can be a potential novel drug dosage form for paediatric, geriatric and also for general population. Finally formulation 4 was considered as optimized formula for preparing FDF of Loratidine, where it shown best drug release profile.

REFERENCES