INTRODUCTION

Recently, the fast dissolving drug delivery system have started gaining popularity and acceptance as they are easy to administer and to achieve better patient compliance (Nagarsenkar et.al 2008). Usually elderly people experience difficulty in swallowing the conventional dosage forms. Fast dissolving film is simply placed on the patient’s tongue, gets rapidly hydrated with saliva, disintegrates and dissolves to release the medication for oromucosal absorption (Pandya et.al 2013). Fast dissolving films disintegrates in 30 s and disappear in 1m by altering the condition of formulation factors, it is possible to speed up or slow down the dissolving rate to meet the need of the end use. By selecting the suitable film ingredients it possible to develop films with the predetermined performance properties.

Alfuzosin Hydrochloride is an alpha-adrenoreceptor blocker is used to relieve symptoms of urinary obstruction in benign prostatic hyperplasia (Debruyne et.al 1998) and also used in the management of hypertension (Mandeep et.al 2013, Buzelin et.al 1993). It is well absorbed from the gastrointestinal tract, but its oral bioavailability is low (49%) due to extensive first pass metabolism. The main objective of present work was to avoid the hepatic first pass metabolism by formulating fast dissolving films by using different polymers.

MATERIALS AND METHODS

MATERIALS

Alfuzosin hydrochloride was a kind gift from Cipla Ltd. India, Hydroxy Propyl Methyl Cellulose E5 and E15 were obtained as gift samples from Colorcon Asia Pvt. Ltd, Mumbai, India. Sorbitol, sodium saccharine, menthol, citric acid and propylene glycol were purchased from S.D fine chemicals Pvt. Ltd., Mumbai. Chemical used were of analytical grade, double distilled water was used throughout the studies.

METHODS

Preparation of fast dissolving films

The fast dissolving films of Alfuzosin Hydrochloride were prepared by using polymers (HPMC E5&E15) by solvent casting method various formulations as shown in Table no1.
Aqueous solution II: It was prepared by dissolving the pure drug, saliva stimulating agents such as citric acid, plasticizer, sweetening agents (sorbitol, sodium saccharine) and flavouring agent (menthol) in specific proportion in distilled water. The aqueous solution I and II were mixed and stirred for 1 h. The solution was cast on to petri dish and were dried in the oven at 45°C for 12 h. The film was carefully removed from surface of petridish and cut according to size required for testing.

Table 1 Composition of Alfuzosin Hydrochloride Fast Dissolving Films.

<table>
<thead>
<tr>
<th>Ingredients (mg)</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>
</tr>
</thead>
<tbody>
<tr>
<td>Alfuzosin HCl</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>HPMC E5</td>
<td>168.3</td>
<td>177.9</td>
<td>187.5</td>
<td>197.2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HPMC E15</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>168.3</td>
<td>177.9</td>
<td>187.5</td>
<td>197.2</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>50.4</td>
<td>53.3</td>
<td>56.2</td>
<td>59.1</td>
<td>50.4</td>
<td>53.3</td>
<td>56.2</td>
<td>59.1</td>
</tr>
<tr>
<td>Sodium saccharine</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Sorbitol</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Citric acid</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>60</td>
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</tr>
<tr>
<td>Menthol</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Water (ml)</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

Physicochemical characterization

Fourier transforms infrared spectroscopy (FTIR)
The infrared spectra of Alfuzosin Hydrochloride, HPMC E5, Physical mixture of Alfuzosin Hydrochloride and HPMCE5 were recorded using Bruker Alpha E, FTIR spectrometers (Bruker Alpha E, Opus-7.0.122 and 8400S, Shimadzu. Japan) equipped with an ATR (Attenuated Total Reflectance). The spectra were scanned at room temperature in transmission mode over the wave number range of 4000- 400 cm⁻¹ (Francesco et.al 2008).

Differential Scanning Calorimetry (DSC)
DSC thermograms of pure drug (Alfuzosin Hydrochloride) and its physical mixture with polymers (HPMC E5& E15) were carried out to investigate any possible interaction between the drug and the utilized polymer ( HPMC E5& E15). The selected heating rate was from 50°C to 300°C at an increase of 20°C per minute. Thermal analysis was performed using a differential scanning calorimetric (8400S Shimadzu. Japan) equipped with a computerized data station (Francesco et.al 2008, Nishimura et.al 2009).

Evaluation of Prepared Films

Thickness
Five strips from the film were randomly taken, thickness of strip was measured by using vernier calipers at different places. Average thickness and standard deviation values were calculated (Chauhan et.al 2012, Raju et.al 2010).

Weight variation
To study the weight variation, individual weights (WI) of strips from each formulation were noted by using electronic balance. Their average weight (WA) was calculated.

Disintegration time
The disintegration time was determined by the following procedure, 10 ml of water was poured in petriplate, and the strip was placed in the centre of the petriplate. The time required for the strip to disintegrate completely was noted. Measurements were carried out in replicates (n=6) and mean±S.D values were recorded.

In vitro drug release studies

In vitro release studies was performed using USP XVIII apparatus I, basket method utilizing dissolution system (Electrolab, India). Shaft speed was maintained at 50 rpm and 900 ml of pH 6.8 phosphate buffer as the dissolution medium at a temperature 37±0.5°C. Samples were collected at pre determined time intervals of 30, 60, 90, 120, 150, 180 s and replaced with equal volume of fresh medium. The solution was filtered and analyzed with UV/Visible spectrophotometer at 243 nm. Concentration of drug calculated from standard calibration curve from that percent drug release was noted (Parthasarathi 2011, Schimoda 2009).

Content uniformity
To determine content uniformity, four strips at different locations were taken from the film and these strips were dissolved in 100 ml of pH 6.8 phosphate buffer solution. The solution was centrifuged at 3000 rpm for 15 m then the supernatant was taken and absorbance was noted spectrophotometrically at 243nm. The drug content was calculated by using the standard calibration curve.

Folding endurance
Folding endurance was measured manually; six strips of dimensions (2X2) cm² were cut from the film. Strips from the film was randomly taken and repeatedly folded at the same place till it breaks. The number of time the strip could be folded gives the value of folding endurance.

RESULTS AND DISCUSSION

Preparation of fast dissolving films

Hydroxy propyl methyl cellulose is a film forming polymer, having excellent film forming ability. To improve the palatability of the fast dissolving films the natural sweeteners are used. Alfuzosin Hydrochloride being bitter in taste; taste masking was achieved by use of sweeteners and flavours. Sorbitol was used as natural sweetener. These agents were expected to give good mouth feel and cooling sensation when incorporated with other sweeteners. Incorporation of mannitol resulted in white patches where as the sorbitol containing films showed good film characteristics. Hence, sorbitol was selected as natural sweetener in this formulation. However one more advantage with sorbitol is its high negative heat of solution. Citric acid was incorporated for its saliva stimulating property. It increases the rate of production of saliva that would assist in the faster disintegration of the film formulations. Propylene glycol was used as a plasticizer to maintain the flexibility of the films.

Thickness
All the formulations were evaluated for the thickness using vernier calipers. The formulations containing different amount of polymers, hence the thickness was gradually increased with
the amount of polymer as shown in figure 1. All the batches were found to have thickness in the range of 0.06 mm to 0.10 mm.

**Disintegration time**

One of the most important characteristics of the fast dissolving films is its disintegration time.

The disintegration test was performed for all the formulations (F1 to F8). The disintegration time was found to be increased with the increase in the concentration of polymer as shown in figure 2. The F1 Formulation consisting of 30% w/w of HPMC E5 disintegrated rapidly within 28.7s than other formulations.

**Folding Endurance**

Formulations with higher amount of polymer showed higher folding endurance values. The formulation F4, F7, F8 showed high folding endurance where as F1, F5, F2 showed lower folding endurance values that can be seen in figure 3.

**Weight variation**

As all batches do not have uniform amount of ingredient in it, hence their weight and thickness were varied. Weight uniformity of the films were found to be between 68.2±0.91mg to 82.2±0.9mg.

**Content uniformity**

The prepared film formulations were analyzed for drug content. Formulations F1 to F8 were showed drug content in range of 95% to 99%. The data for evaluation parameters can be seen in table 2.

**In vitro drug release profile of fast dissolving films at different concentration of HPMC E5**

From figure 4 it is evident that an increase in concentration of polymer resulted in decreased cumulative percent drug release (F2 to F8). Formulation F5 showed drug release of 94.7%, F6, F7 and F8 formulations released only 90.3%, 81.4%, 80.6% of drug within 3 m. This might be due to the increase in concentration polymer, results in formation of strong matrix layer which results in decreased motility of drug particles that leads to decrease in drug release. Where as formulation F1 containing low concentration of polymer as compared to other formulations showed highest drug release of about 100.2% within 3m. The variation in drug release is due to the difference in the viscosity of HPMC E5 and HPMC E15 polymer. HPMC E5 is low viscosity grade polymer hence at low concentration the drug release was found to be high.
Bura Shurthi et al., Oral Fast Disintegrating Films of Alfuzosin hcl

**Physico chemical characterization**

*Fourier Transform Infrared Spectroscopy*

FTIR spectroscopy was employed to ascertain the compatibility of Alfuzosin Hydrochloride with the polymer. The individual drug and drug with polymer were separately scanned as observed in figure 6. FTIR spectra of pure drug showed significant bands at 3348 cm⁻¹ R-NH₂, 3131.3 cm⁻¹ R-NH-R, 1552 cm⁻¹ C-O-C, 1656 cm⁻¹ C=O, 1396 cm⁻¹ C-O-H, 995 cm⁻¹ C-O, which indicates functional groups in match with structure of drug and confirm the purity of the drug. FTIR spectra of HPMC E5 and HPMC E15 polymers showed significant bands at 3350 cm⁻¹ R-NH₂, 1557 cm⁻¹ C-O-C, 1395 cm⁻¹ C-O-H, 997 cm⁻¹ C-O. Both the spectra were compared to confirmation of the common peaks. Alfuzosin Hydrochloride with polymers showed no significant variation in height, intensity and position of the peak, suggesting that the drug and the excipients were compatible. Hence it can be concluded that the drug is in a free state and release easily from the formulation.

**Differential scanning calorimetry (DSC)**

From the figure 7 it can be seen that the thermogram of pure Alfuzosin hydrochloride showed sharp endothermic peak at 238.26°C. Physical mixtures of Alfuzosin hydrochloride with HPMC E5 and E15 respectively also showed sharp endothermic peak of Alfuzosin hydrochloride at 241.35°C. There is no change in endothermic peak of drug which indicates compatibility of HPMC E5 and E15 with drug.

**CONCLUSION**

Fast dissolving films of Alfuzosin Hydrochloride was formulated and evaluated using HPMC E5 & E15 polymer by solvent casting method at 35%, 37%, 39% and 41% w/w. Compatibility of Alfuzosin Hydrochloride and polymer was confirmed by FTIR and DSC studies. The developed films showed excellent uniformity, thickness, dissolution profile and disintegration. Formulation F1 considered as optimum due to its less disintegration time and maximum drug release compare...
to other formulations. From the present research work it can be concluded that the fast dissolving film formulation can be potential drug delivery system for treating benign prostatic hyperplasia with improved patient compliance.

**Conflict of Interest**: The authors declare no conflict of interest

**References**


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