PREPARATION AND EVALUATION OF ORAL FAST DISSOLVING FILMS OF CITALOPRAM HYDROBROMIDE

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ABSTRACT

Fast dissolving film is a dosage form which when placed in the oral cavity, quickly gets hydrated, sticks onto the site of application and then disintegrates to release the drug. Citalopram is an antidepressant also used for mood disorders such as anxiety and obsessive compulsive disorder. Fast dissolving films of Citalopram hydrobromide were prepared by solvent casting technique. HPMC E5 was selected as polymer because of its good water solubility. Propylene glycol as plasticizer and sorbitol as sweetener were used in the formulation. The compatibility of the drug in the formulation was confirmed by FTIR studies. Surfactants by their wetting ability further reduce the disintegration time and enhance the drug release in mouth dissolving films, so tween80 at concentrations of 10%w/w of polymer concentration was included in some formulations. By varying the concentration of polymer and surfactant, four formulations F1, F2, F3 and F4 were formulated. The prepared films were evaluated for their physico-chemical parameters like folding endurance, weight variation, thickness, surface pH, dissolving time and disintegration time. Estimation of drug content of films was performed and the results were satisfactory. Invitro dissolution studies revealed higher drug release from formulations F3 and F4. The order of drug release was found to be F3 > F4 > F1 > F2.

Key words: Fast dissolving film, Citalopram hydrobromide, Tween80, Antidepressant.

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, paediatric and dysphasic patients associated with many medical conditions as they have difficulty in swallowing or chewing solid dosage forms. Even with the fast dissolving tablets there exists a fear of choking due to its tablet type appearance (Habib W et al., 2000; Liang CA and Chen HL, 2001; Anderson O et al., 1995; Joseph F, 2005; Goel Honey et al., 2008; Bhowmik Debjit et al., 2009). 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. Orally fast-dissolving film rapidly disintegrates and dissolves to release the medication for oromucosal and intragastric absorption (Patel RA and Prajapati SD, 2010; Anonymous 1).

Citalopram Hydrobromide is an antidepressant also used for mood disorders such as anxiety and obsessive compulsive disorder. The aim of present work was to improve patient compliance by avoid spitting of the medication by the patients, ensure faster drug delivery for mood disorders, avoid severe gastric irritation and diarrhoea caused by citalopram and mask the bitter taste of drug.

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MATERIALS AND METHODS
Citalopram hydrobromide was obtained as a gift sample from Aurobindo labs, Hyderabad. HPMC E5 was procured from Reddys labs, Hyderabad. Propylene glycol, Sorbitol and Tween80 are purchased from Himedia labs, Mumbai. All the other chemicals used were of analytical grade.

Formulation of Fast Dissolving Films
Fast dissolving films of Citalopram hydrobromide were prepared by solvent casting technique using film forming polymer (Devi K and Paranjothy KL, 1998). Required amount of HPMC E5 according to the formulation table was weighed accurately and soaked aside for 1 hour for swelling of polymer (Aditya Dinge, 2008). Simultaneously Citalopram hydrobromide was weighed accurately and dissolved in 5 ml of distilled water in another beaker. Then drug solution was added to the polymer solution and propylene glycol was added as plasticizer and sorbitol as sweetener and was mixed thoroughly with the help of magnetic stirrer. The above solution was sonicated for 20 min for removal of air bubbles. The glass mould (petridish) having diameter 9 cm was placed over a flat surface and the resulting 10 ml solution with the help of measuring cylinder was transferred into petridish slowly drop by drop and was spread uniformly. Funnel was inverted and placed over the petridish to have uniform evaporation. The petridish containing polymeric solution of drug was kept for 24 hours at room temperature for drying. After drying the films were removed from moulds then similarly formulations F2, F3, F4 were prepared.

Table 1. Formulation of Fast dissolving films of Citalopram hydrobromide

<table>
<thead>
<tr>
<th>S.no</th>
<th>Formulation</th>
<th>Citalopram hydrobromide (mg)</th>
<th>Propylene glycol (ml)</th>
<th>HPMC E5 (mg)</th>
<th>Tween 80 (mg)</th>
<th>Sorbitol (% W/W)</th>
<th>Distilled water qs up to</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F1</td>
<td>63.6</td>
<td>0.5</td>
<td>300</td>
<td>-</td>
<td>0.5</td>
<td>10ml</td>
</tr>
<tr>
<td>2</td>
<td>F2</td>
<td>63.6</td>
<td>0.5</td>
<td>400</td>
<td>-</td>
<td>0.5</td>
<td>10ml</td>
</tr>
<tr>
<td>3</td>
<td>F3</td>
<td>63.6</td>
<td>0.5</td>
<td>300</td>
<td>60</td>
<td>0.5</td>
<td>10ml</td>
</tr>
<tr>
<td>4</td>
<td>F4</td>
<td>63.6</td>
<td>0.5</td>
<td>400</td>
<td>80</td>
<td>0.5</td>
<td>10ml</td>
</tr>
</tbody>
</table>

EVALUATION OF MOUTH DISSOLVING FILMS

Weight variation
For weight variation three films of every formulation were taken weighed individually on digital balance then average weight was calculated.

Film thickness
The thickness of each film was measured using micrometer screw gauge at different positions of the film and the average was calculated.

Surface pH
The film to be tested was placed in a petridish and was moistened with 0.5 ml of distilled water and kept for 1 h. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and kept for 1 min to allow equilibrium condition.

Folding endurance
The folding endurance was determined by repeatedly folding one film at the same place till it broke. The number of times the film could be folded at the same place without breaking gives the value of the folding endurance.

Dissolving time
The dissolving time was determined by placing the film in a beaker containing 50 ml of phosphate buffer (pH 6.8). Time required by the film to dissolve completely was noted.

Drug content
A circular film of 2.5 cm diameter was cut and placed in a beaker. 100 ml of phosphate buffer solution (pH 6.8) was placed. The contents were stirred in magnetic stirrer to dissolve the film. The contents were transferred to a volumetric flask (100 ml). The absorbance of the solution was measured against the corresponding blank solution at 238.5 nm. As the absorbance noted above 1 mcg/ml, 1 ml of the stock was further diluted to 10 ml of phosphate buffer solution (pH 6.8) and absorbance was measured at 238.5 nm.

Disintegration time
Test was performed using disintegration test apparatus. 5 cm² film was placed in the basket, raised and lowered it in such a manner that the complete up and down movement at a rate to achieve equivalent to thirty times a minute. Time required by the film to achieve no trace of film remaining above the gauze was noted (Ajay Kumar Patil, 2011a; Ajay Kumar Patil, 2011b).

In vitro dissolution studies
In vitro dissolution of Citalopram hydrobromide fast dissolving film was studied in USP paddle dissolution test apparatus using phosphate buffer pH 6.8 as the dissolution medium. The temperature was maintained at 37 ± 0.5°C throughout the experiment. 5 ml sample was withdrawn at 50 sec intervals and the same quantity was replaced with phosphate buffer of pH 6.8. The cumulative percentage of drug released was
determined using UV visible spectrophotometer at 238.5 nm.

**RESULTS AND DISCUSSION**

**Preformulation studies**

*Fourier Transform Infra Red Spectroscopy (FTIR)*

The combination spectra of the pure drug and drug with excipients are shown in the figure no.1.

From the FTIR results, it was observed that there exists no physical interaction as there were no changes in the peaks of fingerprint region obtained in the Citalopram Hydrobromide spectrum to that of the spectra of physical mixture of Citalopram Hydrobromide and HPMC E5.

**Weight Variation, Thickness, Surface pH, Folding endurance, Dissolving time, Disintegration time and % Drug content of Citalopram Fast dissolving films:**

The film weight was found to be in the range of 52mg to 62mg which ensured uniform distribution of drug all the formulations. The surface pH of the fast dissolving films which was determined to optimize the drug permeation was found to be in the range of 6.21 to 6.50. It was within the range of salivary pH. Films did not show any cracks even after folding for number of times. All films were having good folding endurance. The results of content uniformity indicated that the drug was uniformly dispersed. Drug content in formulations was uniform with a range of 4.62mg to 4.74mg. Dissolving time for all the films was in the range of 28 to 35 seconds. All the films are disintegrating rapidly. The disintegration time was found to be in the range of 24 to 30 seconds.

**In vitro dissolution studies**

*In vitro* release studies of various formulations were performed using pH 6.8 phosphate buffer as dissolution medium and measuring drug concentration spectrophotometrically at 238.5 nm. The drug release was higher in formulation F3 and F4. The order of drug release was found to be F3 > F4 > F1 > F2. The drug release was more in the films containing tween80. This was because the surfactants cause the wetting of film so that the drug is released rapidly.

![Fig 1. FTIR spectra of A) HPMC E5, B) citalopram hydrobromide, C) physical mixture of citalopram hydrobromide and HPMC E5](image)

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Weight (mg)</th>
<th>Thickness (mm)</th>
<th>Surface pH</th>
<th>Folding endurance</th>
<th>Dissolving time (sec)</th>
<th>Disintegration time (sec)</th>
<th>% Drug content</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>56</td>
<td>0.136</td>
<td>6.51</td>
<td>119</td>
<td>45</td>
<td>27</td>
<td>93.9</td>
</tr>
<tr>
<td>F2</td>
<td>61</td>
<td>0.145</td>
<td>6.72</td>
<td>128</td>
<td>53</td>
<td>30</td>
<td>92.9</td>
</tr>
<tr>
<td>F3</td>
<td>52</td>
<td>0.153</td>
<td>6.45</td>
<td>124</td>
<td>41</td>
<td>24</td>
<td>94.8</td>
</tr>
<tr>
<td>F4</td>
<td>62</td>
<td>0.164</td>
<td>6.83</td>
<td>132</td>
<td>43</td>
<td>25</td>
<td>92.45</td>
</tr>
</tbody>
</table>
CONCLUSION

The present study indicates a good fast dissolving films containing Citalopram hydrobromide for systemic delivery with an added advantage of faster drug action for mood disorders like anxiety and obsessive compulsive disorder. The results of the study show that therapeutic levels of Citalopram hydrobromide can be delivered buccally. It may also be concluded that the presence of tween80 in the formulation enhanced the drug release.

REFERENCES


