Formulation and in vitro evaluation of buccal patches of Desloratidine

M.Jyostna1*, Bhaskar Reddy1, E.Mohanambal1, S.Narendiran3, M.Murugan2, M.Nishanthi4

1Department of Pharmaceutics, Sri Venkateswara College of Pharmacy, Chittoor - 517 127, Andhra Pradesh.
2Department of Pharmaceutics, E.G.S. Pillay College of Pharmacy Nagappatinam - 611001, Tamil Nadu.
3Department of Pharmaceutical Chemistry, Swami Vivekananda Institute of Pharmaceutical Sciences, Vangapally - 508 286, Andhra Pradesh.
4Department of Pharmacognosy, Sri Venkateswara College of Pharmacy, Chittoor -517 127,Andhra Pradesh.

INTRODUCTION

Amongst the various routes of drug delivery, oral route is perhaps the most preferred to the patient and the clinician alike. However peroral administration of drugs has disadvantage such as hepatic first pass metabolism and enzymatic degradation within the GI tract that prohibits oral administration of certain classes of drugs especially peptides and proteins. Consequently, other absorptive mucosae are considered as potential sites for drug administration. Transmucosal routes of drug delivery (i.e., the mucosal lining of the nasal, rectal, vaginal, ocular, and oral cavity) offer distinct advantage over peroral administration for systemic drug delivery. These advantages include possible bypass of first pass effect, avoidance of presystemic elimination within the GI tract, and, depending on the particular drug, a better enzymatic flora for drug absorption.

The nasal cavity has site for systemic drug delivery has been investigated by many research groups and the route has already reached commercial status with several drugs include LHRH and calcitonin. However, the potential irritation and the irreversible damage to the ciliary action of the nasal cavity from chronic application of nasal dosage forms, as well as the large intra- and inter-subject variability in mucus secretion in the nasal mucosa, could significantly affect drug absorption from this site. Even though the rectal, vaginal, and ocular mucosal all offer certain advantages, The oral cavity, on the other hand, is highly acceptable by patients, the mucosa is relatively permeable with a rich blood supply, it is robust and shows short recovery times after stress or damage and the virtual lack of langerhans cells makes the oral mucosa tolerant to potential allergens, furthermore, oral Transmucosal drug delivery bypass first pass effect and avoids presystemic elimination in the GI tract. These factors make the oral mucosal cavity a very attractive and feasible site for systemic drug delivery. Within the oral mucosal cavity, delivery of drugs is classified into three categories; they are Sublingual delivery, buccal delivery, and local delivery. The buccal drug delivery has several advantages which includes bypass of the gastrointestinal tract and hepatic portal system, increasing the bioavailability of orally administered drugs that otherwise undergo hepatic first metabolism, improved patient compliance due to the elimination of associated pain with injections;

Abstract

Buccal patches of Desloratidine were prepared by solvent evaporation method using HPMC 15 cps and xanthan gum which are the hydrophilic polymers in different ratios. The prepared patches were tested for physical parameters like Thickness, Folding endurance, Uniformity of weight, swelling index and Surface pH of patches and in-vitro drug release studies. All the physical parameters were fall within the limits. The drug content was uniform in all the formulated buccal patches of Desloratidine. The results indicate uniform distribution of drug within the patches. The release of Desloratidine from the buccal patch was sustained up to 6hrs. Among the five formulations, the F-V shows maximum drug release of 89.03% in 6 hrs. The optimized formulation follows zero order kinetics to release the drug from the patches.
administration of drugs in unconscious or incapacitated patients, sustained drug delivery, a relatively rapid onset of action can be achieved relative to the oral route, and the formulation can be removed if therapy is required to be discontinued and increased ease of drug administration.

MATERIALS AND METHODS

Materials

Desloratidine was purchased from Microlabs, Hosur, HPMC 15cps was a gift sample from Signet chemicals, Mumbai, Xanthan gum was purchased from Signet chemicals, Mumbai Glycerine was purchased from Spectrum reagents & chemicals private ltd, Chennai and Propylene glycol was purchased from SD Fine Chemicals, Boisar. All the excipients and solvents used were of analytical grade.

Methods

Drug Excipient compatibility study

Fourier Transform Infrared Spectroscopy

Excipients are integral components of almost all pharmaceutical dosage forms. The successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients, which are added to facilitate administration, promote the consistent release and bioavailability of the drug and protect it from degradation.

Infra Red spectroscopy is one of the most powerful analytical techniques to identify functional groups of a drug.

Method

The pure drug and its formulation were subjected to IR studies. In the present study, the potassium bromide disc (pellet) method was employed. A physical mixture (1:1) of drug and polymer was prepared and mixed with suitable quanta of potassium bromide. About 100 mg of this mixture was compressed to from a transparent pellet using a hydraulic press at 10 tons pressure. It was scanned from 4000 to 400 cm⁻¹ in a Shimadzu FTIR 8400 Spectrophotometer. The IR spectrum of the physical mixture was done to detect any appearance or disappearance of peaks. The compatibility between the drug and the polymer were evaluated using FTIR matching method.

Formulation of Buccal patches of Desloratidine

Buccal patches of Desloratidine were prepared by solvent casting technique using film forming polymers such as HPMC and Xanthan gum. HPMC polymer was weighed accurately and dissolved in 2 ml of ethanol. The beaker containing polymer and ethanol was kept aside for 5 min for swelling of the polymer. Further 3 ml of ethanol was added to the above polymer solution and the dispersion was stirred. Then one drop of glycerine was added to the polymer solution. Accurately weighed Desloratidine was dissolved in 1 ml of ethanol in another beaker. The drug solution was added to the polymer solution and was mixed thoroughly with the help of a magnetic stirrer. The resulting viscous solution was casted into petridish and dried in an oven at 50°C for 48 hours. The dried films were carefully removed and checked for any imperfection or air bubbles. The patches were packed in an aluminium foil and stored in an air tight glass container to maintain the integrity and elasticity of the patches.

Table 1: Composition of different Buccal mucoadhesive formulations containing Desloratidine

<table>
<thead>
<tr>
<th>Composition</th>
<th>Formulation code</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F-I</td>
</tr>
<tr>
<td>Desloratidine (mg)</td>
<td>5</td>
</tr>
<tr>
<td>HPMC 15cps (mg)</td>
<td>-</td>
</tr>
<tr>
<td>Xanthan gum (mg)</td>
<td>100</td>
</tr>
<tr>
<td>Glycerine (ml)</td>
<td>0.02</td>
</tr>
<tr>
<td>Ethanol (ml)</td>
<td>7</td>
</tr>
<tr>
<td>Propylene glycol (ml)</td>
<td>0.2</td>
</tr>
<tr>
<td>Sod. Saccharine (mg)</td>
<td>0.01</td>
</tr>
<tr>
<td>Water</td>
<td>q.s</td>
</tr>
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</table>
Physical characterization of buccal patches

Thickness of the patches
The thickness of the patches was evaluated by taking three patches of each formulation and the patch thickness was measured using the Vernier calipers instrument at three different places and the mean value was calculated.

Folding endurance
Three patches of each formulation of size (2x2 cm) were cut by using sharp blade. Folding endurance was determined by repeatedly folding a small strip of patch at the same place till it broke. The number of times, the patch could be folded at the same place without breaking gave the value of folding endurance. The mean value was calculated.

Uniformity of weight of the patches:
Uniformity of weight of the patches was measured by taking three patches of each formulation and weighed individually on a digital balance. The average weight was calculated.

Drug content uniformity of the patches:
The three patches (2x2 cm) of each formulation were taken in separate 100 ml volumetric flasks, 100 ml of pH 6.8 phosphate buffer was added and continuously stirred for 24 hrs. The solutions were filtered, diluted suitably and analyzed at 241 nm in a UV spectrophotometer.

Swelling index:
The degree of swelling of bio adhesive polymer is an important factor affecting adhesion. Upon application of the bio adhesive material to a tissue a process of swelling may occur. The patches were allowed to swell on the surface of agar plate kept in an incubator maintained at 37±0.2°C. Increase in the weight of the patch was determined at preset time intervals (1-3 hrs). The percent swelling of the patches was calculated using the formula

% S = (Xt – X0/X0) x 100,

Where,
Xt is the weight of swollen patch after time t,
X0 is the initial patch weight at zero time.

Surface pH of patches:
The patches were allowed to swell by keeping them in contact with 1 ml of distilled water (pH 6.8±0.1) for 2 hrs at room temperature, and pH was noted down by bringing the electrode in contact with the surface of the patch, allowing it to equilibrate for 1 minute. The surface pH of the patches was determined in order to investigate the possibility of any side effects, in the oral cavity. As acidic or alkaline pH is bound to cause irritation to the buccal mucosa, hence attempt was made to keep the surface pH of the patch close to the neutral pH.

In-vitro drug release studies

In-vitro drug release studies were carried out using USP dissolution test apparatus type II (Electrolab dissolution Tester). The in-vitro release studies were carried out by using 900 ml of isotonic phosphate buffer (pH 6.8) as the dissolution medium at 37±0.5°C and 50 rpm. To provide unidirectional release, one side of buccal patch was attached to a glass disk with the help of two sided adhesive tape. The disk was introduced in the bottom of the dissolution vessel such that patch surface is exposed to the dissolution medium. An aliquot of 5ml sample was withdrawn at predetermined time intervals and similar volume was replaced with fresh phosphate buffer (pH 6.8) maintained at same temperature. Samples were then analyzed spectrophotometrically at 241 nm.

Drug release kinetics-model fitting of the dissolution Data:
Whenever a new solid dosage form is developed or produces, it is necessary to ensure that drug dissolution occurs in an appropriate manner. Nowadays the pharmaceutical industry and the registration authorities focus on drug dissolution studies. Drug dissolution from buccal patches has been described by kinetic models in which the dissolved amount of drug (Q) is a function of the test time, t or Q = f (t). Some analytical definitions of the Q(t) function are commonly used such as zero order, first order, Higuchi, Korsmeyers models.

The results of In-vitro release profile obtained for all the formulations were plotted in modes of data treatment as follows.
1. Log cumulative percent drug remaining versus time (first order kinetic model)
2. Cumulative percent drug release versus square root of time (Higuchi’s model)
3. Log cumulative percent drug release versus time (zero order kinetic model)
4. Log cumulative Percent Drug released versus log time (korsmeyers model)
RESULTS AND DISCUSSION

Drug Excipient Compatibility Study

IR spectra of Desloratidine alone and its combination with polymers are evaluated. An IR spectrum of pure Desloratidine showed the peaks 3311.7 cm⁻¹ (N-H, str), 3060.6 cm⁻¹ (C-H, str, Sp²), 2923.56 cm⁻¹ (C-H, str, Sp³), and 1316.1 cm⁻¹ (C-O, str). The IR peaks of drug and polymer separately shown in figure.1 & figure.2 respectively. These peaks can be considered as characteristic peaks of Desloratidine and were not affected and prominently observed in IR spectra of Desloratidine along with polymers as shown in the fig.3, indicated no interaction between Desloratidine and polymers.

Figure.1 IR SPECTRUM OF COMPOUND-(DESLORATIDINE)-A₁

Figure.2 IR SPECTRUM OF COMPOUND (HPMC)-A₂

Figure.3 IR SPECTRUM OF COMPOUND (DESLORATIDINE+HPMC)-A₃
Physical characterization of buccal patches

The physical characterization of the formulated buccal patches were done by various techniques mentioned and the results were tabulated in Table no: 2 for various parameters like thickness of the patches, folding endurance, uniformity of weight of the patches, drug content uniformity of the patches, swelling index, surface pH of patches.

<table>
<thead>
<tr>
<th>Formulation</th>
<th>TN (mean±Std)</th>
<th>UW (mean±Std)</th>
<th>%SI (mean±Std)</th>
<th>Surface pH (mean±Std)</th>
<th>CU (mean±Std)</th>
<th>FE (mean±Std)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F-I</td>
<td>0.204±0.001</td>
<td>22.43±1.17</td>
<td>46.00±1.53</td>
<td>6.7±0.120</td>
<td>88.30±0.05</td>
<td>152</td>
</tr>
<tr>
<td>F-II</td>
<td>0.179±0.002</td>
<td>18.48±1.32</td>
<td>32.17±1.78</td>
<td>6.45±0.160</td>
<td>98.74±0.44</td>
<td>188</td>
</tr>
<tr>
<td>F-III</td>
<td>0.189±0.001</td>
<td>16.37±1.34</td>
<td>34.13±1.39</td>
<td>6.86±0.170</td>
<td>99.16±0.46</td>
<td>169</td>
</tr>
<tr>
<td>F-IV</td>
<td>0.250±0.001</td>
<td>29.34±1.26</td>
<td>48.34±1.05</td>
<td>6.80±0.135</td>
<td>93.25±0.047</td>
<td>190</td>
</tr>
<tr>
<td>F-V</td>
<td>0.198±0.002</td>
<td>23.35±1.69</td>
<td>30.40±1.29</td>
<td>6.73±0.156</td>
<td>99.62±0.62</td>
<td>200</td>
</tr>
</tbody>
</table>

TN= thickness, UW= uniformity of weight, SI= percent swelling index, CU = content uniformity, and FE = folding endurance respectively. *Each value is an average of three determinations.

The release data of Desloratidine from all the patches is shown in Table 3 & fig. 4 at Isotonic Phosphate pH 6.8, HPMC is present in the ionized state and as a result the polymeric network gets loosened comparatively, attributing for the higher drug release. An increase in the polymer HPMC content was associated with a corresponding decrease in the drug-release rate. The drug release was observed to be sustaining with increasing the incorporation of higher amount of HPMC in patch F-V. This could be due to the extensive swelling of the polymers, which created a thick gel barrier for drug diffusion. The drug release was increased...
linearly with the increasing concentration of HPMC (Hydrophilic polymer), as it was observed in patch F-V which showed maximum release 89.03% in 6 hrs among other patches.

Table: 3 In-vitro Dissolution Studies of Buccal patches Containing Desloratidine

<table>
<thead>
<tr>
<th>S.No</th>
<th>Time</th>
<th>F-I</th>
<th>F-II</th>
<th>F-III</th>
<th>F-IV</th>
<th>F-V</th>
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<tbody>
<tr>
<td>1</td>
<td>0.5</td>
<td>36.96</td>
<td>35.55</td>
<td>34.95</td>
<td>33.12</td>
<td>38.17</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>38.97</td>
<td>37.17</td>
<td>41.4</td>
<td>41.57</td>
<td>44.83</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>44.01</td>
<td>43.62</td>
<td>45.04</td>
<td>47.49</td>
<td>46.85</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>49.68</td>
<td>47.26</td>
<td>49.47</td>
<td>51.73</td>
<td>60.57</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
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<td>51.69</td>
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<td>58.46</td>
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</tr>
<tr>
<td>6</td>
<td>5</td>
<td>61.11</td>
<td>56.34</td>
<td>59.16</td>
<td>60.94</td>
<td>78.57</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>69.84</td>
<td>64.81</td>
<td>67.84</td>
<td>68.29</td>
<td>89.03</td>
</tr>
</tbody>
</table>

Figure: 4 In vitro release profile of Buccal patches Containing Desloratidine

Figure: 5 Cumulative percent drug release Vs Time Plot
Mechanism of release

Data of the in vitro release were fitted into different equations and kinetic models to explain the release kinetics of Desloratidine from these buccal patches. The kinetic models used were zero-order equation, first order equation, Higuchi release, and Korsmeyer-Peppas models. The interpretation of data was based on the value of the resulting regression coefficients. The dissolution data was best fitted to Zero order which is used to describe the drug release behaviour from polymeric system.

CONCLUSION

The present study clearly demonstrated that Desloratidine can be successfully delivered through buccal route. IR spectroscopic studies indicated that the drug is compatible with the polymer. A buccal patch of Desloratidine was formulated by using a hydrophilic polymer HPMC 15 cps and prepared by Solvent casting method were found to be good in appearance. The formulated buccal patches were evaluated for the Physical parameters like thickness, Folding endurance, Uniformity of weight, swelling Index, Surface pH. The results obtained were within the prescribed limits. The patches were non-irritating with favourable film properties and showed sufficient mucoadhesive potential until the drug is absorbed from the formulation. So, it can be concluded that buccal patches of HPMC meets the ideal pre-requisites for a buccal device which can be a good way to by-pass hepatic first pass metabolism of Desloratidine.

Acknowledgement

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