FORMULATION AND IN-VITRO DRUG RELEASE STUDIES OF OXICONAZOLE NITRATE TRANSDERMAL PATCHES

Nageswara Rao. G* and Rama Krishna. A

Department of Pharmaceutical Chemistry, Telangana University, Nizamabad, Andhra Pradesh-503322, India

*Corresponding author (pharmajntu@gmail.com)

ABSTRACT: The present study transdermal patches of the Oxiconazole Nitrate were prepared using polymers like Hydroxypropyl methylcellulose, sodium carboxy methyl cellulose and carbopol 934 with different concentration. The patches (1cm2) were cut and added to a beaker containing 100 mL of phosphate buffered saline10 of pH 7.4. The medium was stirred with magnetic bead. The contents were filtered using whatmann filter paper and the filtrate was examined for the drug content against the reference solution consisting of placebo patches (contains no drug) at 274 nm spectrophotometrically. The patches prepared from HPMC and carbomer (H4 and H5) show more tensile strength than the patches prepared from SCMC and carbomer (H8 and H10). As the concentration of hydrophilic polymer HPMC, SCMC and carbomer were increased there is increase in tensile strength, folding endurance of patches between 74.11 ± 4.231 to 97.56 ± 6.231, drug content uniformity and in vitro release studies.

Keywords: Oxiconazole Nitrate, transdermal patches, HPMC, sodium carboxy methyl cellulose.

INTRODUCTION

Transdermal drug delivery systems (TDDS) are adhesive drug containing devices of defined surface area that delivers predetermined amount of drug to the intact skin at a pre-programmed rate. The transdermal delivery has gained importance in recent years [1]. The transdermal drug delivery system has potential advantages of avoiding hepatic first pass metabolism, maintaining constant blood levels for longer period of time resulting in a reduction of dosing frequency, improved bioavailability decreased gastrointestinal irritation that occur due to local contact with gastric mucosa, and improved patient compliance. Some of the anti hypertensive drugs already have been formulated and evaluated as transdermal patches but most of them still been unexplored [2].
Transdermal formulation of anti fungal drug is promising aspect in near future. Controlled drug release can be achieved by transdermal drug delivery systems (TDDS) which can deliver medicines via the skin portal to systemic circulation at a predetermined rate over a prolonged period of time 1-3. TDDS has gained a lot of interest during the last decade as it offers many advantages over the conventional dosage forms and oral controlled release delivery systems notably avoidance of hepatic first pass metabolism, less frequency of administration, reduction in gastrointestinal side effects and improves patient compliance. For transdermal products the goal of dosage design is to maximize the flux through the skin into the systemic circulation and simultaneously minimize the retention and metabolism of the drug in the skin. Most treatments are either systemic antifungal medications, such as Oxiconazole Nitrate [3].

MATERIAL AND METHODS

Material

Oxiconazole Nitrate was received as a gift samples from Taj Pharmaceuticals Limited, Mumbai, India. Hydroxypropyl methylcellulose (HPMC) and sodium carboxy methyl cellulose (SCMC) and carbopol 934 were procured from Merk, Mumbai, India, respectively. Glycerol was procured from S.D Fine chemical Ltd. (Mumbai, India). All other laboratory chemicals used in the study were of analytical reagents grade. Double distilled water was used throughout the study. The chemical structure of Oxiconazole Nitrate.

\[ \text{Fig. 2: Chemical Structure of Oxiconazole Nitrate} \]

Method Preparation of Transdermal Patches

Different formulation were prepared with various ratio of (HPMC: carbomer), (SCMC: carbomer), (HPMC: SCMC),(HPMC: SCMC: carbomer). Many experiments were conducted by varying the concentrations of those polymers in order to identify the optimum concentration required for polymer solution [4].

**Step I:** Required quantity of HPMC, SCMC and carbomer 934 was soaked in sufficient quantity of distilled water and kept overnight for swelling.

**Step II:** The polymer solutions were mixed with magnetic stirrer, until a uniform solution was obtained.

**Step III:** An appropriate amount of Oxiconazole Nitrate was solubilized in above polymer solution with continuous stirring until an uniform solution obtained.

**Step IV:** Then the polymer solutions was poured in to a petridish on level surface and allowed to evaporate at controlled rate by covering the petridish with funnel to avoid blistering effect after drying of patches [5] [16].

<table>
<thead>
<tr>
<th>S.No</th>
<th>Ingredient (g)</th>
<th>H1</th>
<th>H2</th>
<th>H3</th>
<th>H4</th>
<th>H5</th>
<th>H6</th>
<th>H7</th>
<th>H8</th>
<th>H9</th>
<th>H10</th>
<th>H11</th>
<th>H12</th>
<th>H13</th>
<th>H14</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Oxiconazole Nitrate</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>2</td>
<td>HPMC</td>
<td>0.1</td>
<td>0.2</td>
<td>0.3</td>
<td>0.4</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.1</td>
<td>0.2</td>
<td>0.3</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>3</td>
<td>SCMC</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.1</td>
<td>0.2</td>
<td>0.3</td>
<td>0.1</td>
<td>0.2</td>
<td>0.3</td>
<td>0.3</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>4</td>
<td>Carbomer 934</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>5</td>
<td>Glycerol (%)</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>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>Distilled water (ml)</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>

SCMC- sodium carboxy methyl cellulose
HPMC- hydroxypropyl methyl cellulose
Tensile Strength

Tensile strength of the film was determined with Universal strength testing machine (Hounsfield, Slinfold, Horsham, U.K.). The sensitivity of the machine was 1 g. It consisted of two load cell grips. The lower one was fixed and upper one was movable. The test film of size (4×1cm²) was fixed between these cell grips and force was gradually applied till the film broke. The tensile strength of the film was taken directly from the dial reading in kg [6] [15].

Tensile strength is expressed as follows:

\[ \text{Tensile strength} = \frac{\text{Tensile load at break}}{\text{Cross section area}} \]

Drug Content Uniformity of Patches

The patches (1cm²) were cut and added to a beaker containing 100 mL of phosphate buffered saline of pH 7.4. The medium was stirred with magnetic bead. The contents were filtered using whatmann filter paper and the filtrate was examined for the drug content against the reference solution consisting of placebo patches (contains no drug) at 274 nm spectrophotometrically. The experiment was repeated to validate the result [7] [14].

In Vitro Drug Release Studies

In vitro skin permeation studies were performed by using a modified Franz diffusion cell with a receptor compartment capacity of 20 ml. The synthetic cellophane membrane was mounted between the donor and receptor compartment of the diffusion cell [8] [13]. The formulated patches were cut into size of 1cm² and placed over the drug release membrane and the receptor compartment of the diffusion cell was filled with phosphate buffer pH 7.4 [8] [12]. The whole assembly was fixed on a magnetic stirrer, and the solution in the receptor compartment was constantly and continuously stirred using magnetic beads at 50 rpm; the temperature was maintained at 37 ± 0.5°C [9]. The samples of 1 ml were withdrawn at time interval of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 14 hrs. The receptor phase was replenished with an equal volume of phosphate buffer at each time of sample withdrawal. The cumulative amounts of drug permeated per square centimeter of patches were plotted against time [10] [11].

Table 2. Results of Tensile Strength, Drug Content and in vitro Drug Release

<table>
<thead>
<tr>
<th>S.No</th>
<th>Tensile Strength (Kg/mm²)</th>
<th>% Drug Content</th>
<th>% Drug Release</th>
</tr>
</thead>
<tbody>
<tr>
<td>H4</td>
<td>3.91 ± 0.032</td>
<td>92.01</td>
<td>96.21 ± 4.231</td>
</tr>
<tr>
<td>H5</td>
<td>3.87 ± 0.013</td>
<td>90.21</td>
<td>97.56 ± 6.231</td>
</tr>
<tr>
<td>H8</td>
<td>3.21 ± 0.114</td>
<td>92.11</td>
<td>74.11 ± 4.231</td>
</tr>
<tr>
<td>H10</td>
<td>3.31 ± 0.012</td>
<td>92.42</td>
<td>74.34 ± 8.220</td>
</tr>
<tr>
<td>H13</td>
<td>4.62 ± 0.111</td>
<td>93.01</td>
<td>82.14 ± 6.241</td>
</tr>
<tr>
<td>H14</td>
<td>4.53 ± 0.043</td>
<td>93.22</td>
<td>82.23 ± 5.247</td>
</tr>
</tbody>
</table>

Fig.3. Showing the Diffusion of Optimized Formulation
RESULTS AND DISCUSSION

The transdermal patches were transparent, smooth, uniform and flexible. The patches prepared from HPMC and carbomer (H4 and H5) show more tensile strength than the patches (Table 2) prepared from SCMC and carbomer (H8 and H10). As the concentration of hydrophilic polymer HPMC, SCMC and carbomer were increased there is increase in tensile strength. The tensile strength measures the ability of patches to withstand rupture. The mean value was found to vary between 3.21 ± 0.114 to 4.62 ± 0.111 kg/mm². The drug content of each formulation (Table 1) was evaluated and the results are shown in Table 2. Drug content in all formulations were found to be uniform ranging from 92.01 to 93.22%. This indicates that the drug was dispersed uniformly throughout the patches. Release studies are required for predicting the reproducibility of rate and duration of drug release. The importance of polymer diffusion on drug release from matrices has been known for ensuring the sustained release performance. The result indicated that the release of drug from patches increases with increasing concentration of HPMC with carbomer. The cumulative percent of drug release in 14 h was found to be the highest (82.23 ± 5.247) from formulation H14 carrying HPMC, SCMC and carbomer (Fig 3) and minimum (74.11 ± 4.231) from formulation H8 carrying SCMC and carbomer.

CONCLUSION

From the results obtained and discussion generated there from, encouraged conclusions were drawn. On the basis of the in vitro characterization it was concluded that Oxiconazole could be administered transdermally through matrix type TDDS developed in our laboratory. Transdermal patches consisting of the bioadhesive polymers HPMC, SCMC and cabomer 934 with Oxiconazole Nitrate were effective for nail fungal infection. The drug remained intact and stable in the TDDS during storage, with no significant chemical interaction between the drug and the excipient.

REFERENCES