Formulation and Evaluation of Valdecoxib gel for Topical Administration

INTRODUCTION

The utilization of non-steroidal anti-inflammatory drugs is perfectly known for regional inflammatory disorders such as muscle pain and osteoarthritis. Valdecoxib, a specific COX2 inhibitor, is one of the most potent non-steroidal anti-inflammatory agents. It was approved by for the treatment of pain and inflammation associated with musculoskeletal disorders. Its oral bioavailability is 93% but reaches steady state plasma concentration at 3-4 days with multiple dose oral administration [1].

Delivery of drugs to the skin is an effective and targeted therapy for local dermatological disorders [2]. This route has gained popularity since it avoids first pass metabolism and gastrointestinal irritation associated with oral administration [3]. Due to the first past effect, only less amount of the oral administered dose reaches the blood circulation which can be bypass by the gel formulations as topical application. Topical gel formulations provide a suitable delivery system for drugs because they are less greasy and can be easily removed from the skin.

The release of the drug from topical preparations depends on the physicochemical properties of the vehicle and the drug employed. Gel base formulation makes the drug molecules more easily removable from the system then cream and ointment [4, 5]. Gels for dermatological use have several favorable properties such as being greaseless, easily spreadable, easily removable, emollient, compatible with several excipients and water-soluble or miscible [6].

Drug delivery via skin has a potential view for a long time because skin is easy to access with large surface area and the route is noninvasive. Topical gel preparations are proposed for external application or to some mucosal surfaces for local action or skin penetration of medicament or for their soothing or protective action.

The aim of this study was to develop suitable topical gel formulations of valdecoxib using different gelling agent with permeation enhancers in order to reduce adverse drug reaction associated with oral formulations.

MATERIALS AND METHODS

Materials

Valdecoxib was a gift sample from Alembic Pharmaceutical Ltd. Carbopol 934, HPMC K4M, Glycerin, Triethanolamine, Methyl paraben and
potassium dihydrogen phosphate were purchased from CDH, New Delhi, India.

Methods
Gels were prepared by dispersing the polymers in a mixture of water and glycerol with methylparaben as preservative and varying amount of valdecoxib, being kept under magnetic stirring until homogeneous dispersion was formed. The dispersion was then neutralized and made viscous by the addition of triethanolamine and glycerol respectively. The compositions of different gel formations are listed in Table 1.

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valdecoxib (mg)</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Carbopol-934 (%w/v)</td>
<td>1.5</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HPMC K4M (%w/v)</td>
<td>-</td>
<td>-</td>
<td>1.5</td>
<td>2</td>
</tr>
<tr>
<td>Triethanolamine (ml)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Glycerol (mg)</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Methyl Paraben</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Characterization of Formulations
The prepared valdecoxib gels were inspected visually for their homogeneity, grittiness, viscosity, Spreadability, pH, drug content and in vitro drug release.

Homogeneity: All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates.

Grittiness: All the formulations were evaluated microscopically for the presence of particles if any no appreciable particulate matter was seen under light microscope. Hence obviously the gel preparation fulfils the requirement of freedom from particular matter and from grittiness as desired for any topical preparation.

Viscosity: The measurement of viscosity of the prepared gel was done with a Brookfield viscometer. The gels were rotated at 20 and 30 rpm using spindle no. 64. At each speed, the corresponding dial reading was noted [7].

Spreadability: Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel and placed in between the slides under the direction of certain load, lesser the time taken for separation of two slides, better the spreadability. It is calculated by using the formula:

\[ S = \frac{M \times L}{T} \]

Where M = weight tied to upper slide
L = length of glass slides
T = time taken to separate the slides

pH: The pH was measured in each gel, using a pH meter, which was calibrated before each use with standard buffer solutions at pH 4, 7, 9. The electrode was inserted in to the sample 10 min priors to taking the reading at room temperature.

Drug content: To ensure uniform formulation of the gel, it was sampled from the different locations in the mixer and assayed for the drug content. Drug content of the gels was determined by dissolving an accurately weighed quantity of gel (about 1 gm) in about 100 ml of pH 6.8 phosphate buffer. These solutions were quantitatively transferred to volumetric flasks and appropriate dilutions were made with the same buffer solution. The resulting solutions were then filtered 0.45 mm membrane filters before subjecting the solution to spectrophotometric analysis.

In vitro diffusion studies: The in vitro diffusion studies of prepared gel were carried out in Franz diffusion cell using through a cellophane membrane.100 ml of phosphate buffer was used as receptor compartment, then 500 mg of gel containing 10 mg of valdecoxib was spread uniformly on the membrane. The donor compartment was kept in
contact with a receptor compartment and the temperature was maintained at 37±0.50. The solution on the receptor side were stirred by externally driven Teflon coated magnetic bars at predetermined time intervals, pipette out 5ml of solution from the receptor compartment and immediately replaced with the fresh 5ml phosphate buffer. The drug concentration on the receptor fluid was determined spectrophotometrically against appropriate blank. [8] The experiment was carried out in triplicate.

**Table 2**: Evaluation Table for Valdecoxib loaded Gel Formulation

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Homogeneity</th>
<th>Grittiness</th>
<th>pH</th>
<th>Viscosity (cps)</th>
<th>Spreadability (gm X cm/Sec)</th>
<th>Drug Content (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>++</td>
<td>--</td>
<td>7.21</td>
<td>1425.45</td>
<td>32.93</td>
<td>99.01</td>
</tr>
<tr>
<td>F2</td>
<td>++</td>
<td>--</td>
<td>7.26</td>
<td>1172.89</td>
<td>26.29</td>
<td>102.46</td>
</tr>
<tr>
<td>F3</td>
<td>++</td>
<td>--</td>
<td>7.12</td>
<td>1025.67</td>
<td>21.37</td>
<td>101.34</td>
</tr>
<tr>
<td>F4</td>
<td>++</td>
<td>--</td>
<td>6.89</td>
<td>1943.78</td>
<td>22.45</td>
<td>99.37</td>
</tr>
</tbody>
</table>

(++) indicates good Homogeneity, -- indicates no grittiness)

**Figure 1**: In vitro Drug Diffusion Profiles of all Gel Formulations

**REFERENCES**


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