Preparation and evaluation of transdermal patch of Aceclofenac


1Department of Pharmaceutical Sciences, University of Kashmir, Srinagar, J&K, India.
2Department of Pharmacetics, Jamia Hamdard, New Delhi, India.
3Department of Education, J&K, India

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ABSTRACT

The matrix type Transdermal drug delivery system of aceclofenac was prepared by film casting technique employing mercury as the substrate & characterized by in-vitro drug release and in-vitro skin permeation studies. Four formulations were developed which differed in the ratio of polymers. Films having polymer ratio of 4:1 with respect to Eudragit RL100 and Polyvinpyrrolidone, containing 2% Brij-58 as penetration enhancer were selected as optimized formulations. Cumulative amount of drug released and permeated from the optimized formulation were found to be 69.63% and 70.92% respectively.

Keywords: Aceclofenac, Transdermal Therapeutic System, In-vitro Permeation, Surfactant.

INTRODUCTION:

NSAIDs are amongst the most widely used of all therapeutic agents. They are frequently prescribed for the long-term treatment of rheumatic musculoskeletal complaints. These are the drugs of first choice for the management of variety of chronic orthopedic ailments.

The major drawback of anti-inflammatory drug use is the occurrence of gastrointestinal side effects. As these drugs are generally given for a longer duration of time, they cause gastrointestinal disturbances which are generally recognized to be due to interference by the drug with the biosynthesis of prostaglandins and other arachidonic acid metabolites in the gastric mucosa. These drugs also undergo substantial hepatic first pass metabolism and only small fraction of the drug reaches systemic circulation. This originates the need of an alternative route of administration, which can bypass the gastrointestinal metabolism of the drug and hence desired plasma concentrations could be achieved.

METHODOLOGY:

The mercury surface was selected for film formation [1-3]. Plasticizers and polymers were dissolved in the solvent and poured into the film casting assembly i.e. glass rings placed on the surface of mercury in a petridish. Solvent was allowed to evaporate by placing an inverted funnel over the petridish which controlled the rate of evaporation of the solvent. The dried films were removed from the glass ring and kept in a desiccator until use. To determine the optimum combination of polymers, plasticizer and solvent, films were formulated using them in different ratios [Table-1].

Calculation of dose:

Transdermal dose can be calculated with help of following formula [8]:

\[
\text{Transdermal dose} = \text{Oral dose} \times \text{Bioavailability}
\]

The usual oral dose of Aceclofenac is 50-100mg daily and the bioavailability is 50% approximately. Therefore, the calculated transdermal dose based upon highest oral dose is 50 mg daily.

Table 1: Formulae for films using Eudragit RL 100 and Polyvinyl pyrrolidone with enhancer (2% w/w Brij 58)

<table>
<thead>
<tr>
<th>Code</th>
<th>RL100 (mg)</th>
<th>PVP K30 (mg)</th>
<th>Propylene PEG-400 (w/w)</th>
<th>Brij 58 (w/w)</th>
<th>Chloroform (ml)</th>
<th>Area of casting ring (cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>100</td>
<td>400</td>
<td>20</td>
<td>20</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>P2</td>
<td>200</td>
<td>300</td>
<td>20</td>
<td>20</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>P3</td>
<td>300</td>
<td>200</td>
<td>20</td>
<td>20</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>P4</td>
<td>400</td>
<td>100</td>
<td>20</td>
<td>20</td>
<td>2</td>
<td>10</td>
</tr>
</tbody>
</table>

In-Vitro Drug Release Studies:

The in vitro drug release studies on Aceclofenac were performed using paddle-over-disc assembly specified in USP. The vessel of the dissolution apparatus was filled with 900 ml of (IPB) isotonic phosphate buffer (pH 7.4) and the assembly was equilibrated to 32 ± 0.5°C. The patch of specified area was placed on a teflon disc. The disc was placed flat at the bottom of the USP Apparatus 2. The study was performed at 50 rpm, 5 ml aliquot, which was replaced by fresh media, was collected at intervals for 24h. The collected samples were analyzed by UV spectrophotometer at ?max of 276 nm.

In-Vitro Skin Permeation Studies:

i) Fabrication of diffusion cell:

Keshary and Chien cell was used for permeation studies. The vertical double walled diffusion cell, consisted of two half cells and area of diffusion between the two half cells was 12 cm² and the capacity of receiver chamber was 80 ml. The skin sample was sandwiched between the two half- cells with stratum corneum facing, the donor compartment. The whole assembly was maintained at 37 ± 1°C[6-7].

ii) Procedure:

The skin was excised from albino rat, pretreated and stabilized. Transdermal patch was placed in the donor compartment in such a way that the release surface of the system faced the stratum corneum. The receiver cell was filled with IPB (pH 7.4). The patch of specified area was placed between the two half cells with release surface facing the donor compartment. A teflon bead was maintained at 50 rpm in the receiver chamber. The samples (1ml) were withdrawn at regular interval (1, 2, 3, 4, 5, 6, 8, 10, 12, 22 and 24 h), filtered and analyzed for drug content by UV spectrophotometer. Permeated studies are shown in [Tables-2].

*Corresponding author.*

Mudasir Mohamad,
Department of Pharmaceutical Sciences,
Kashmir University-190006, J& K, India
Tel.: + 91-9622694575
E-mail: mudasirmohamad@gmail.com
RESULTS AND DISCUSSION:
From the In-vitro drug release and In-vitro permeation studies, it was revealed that highest cumulative amount of drug released from the patch formulation was 69.63% and highest cumulative amount of drug permeated was 70.92% from the optimized formulation (Eudragit RL100% PVP; 4:1). Brij-58 (2% w/w) showed the highest cumulative percentage permeated among all the enhancers. An increased % drug release & permeation was obtained upon increasing the concentration of Eudragit RL 100, suggesting that its major influence on the drug release and permeation with the increase in the quantity Table-2: In vitro permeation of aceclofenac patch (P4) with permeation enhancer (2% Brij 58).

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Mean Absorbance (±SD)</th>
<th>Concentration (µg/ml)</th>
<th>Cumulative amount of drug permeated (mg)</th>
<th>Cumulative % of drug permeated</th>
<th>Flux (mg/cm²/h)</th>
<th>Pbx10⁻³ (cm/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.398±0.016</td>
<td>8.918</td>
<td>0.810</td>
<td>14.353</td>
<td>0.1318</td>
<td>0.0228</td>
</tr>
<tr>
<td>2</td>
<td>0.453±0.013</td>
<td>10.109</td>
<td>0.919</td>
<td>16.270</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0.528±0.014</td>
<td>11.734</td>
<td>1.066</td>
<td>18.884</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>0.585±0.014</td>
<td>12.968</td>
<td>1.178</td>
<td>20.870</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.644±0.017</td>
<td>14.246</td>
<td>1.295</td>
<td>22.927</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>0.692±0.013</td>
<td>15.286</td>
<td>1.389</td>
<td>24.600</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>0.811±0.014</td>
<td>17.863</td>
<td>1.623</td>
<td>28.748</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0.913±0.017</td>
<td>20.072</td>
<td>1.824</td>
<td>32.303</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>1.114±0.016</td>
<td>24.425</td>
<td>2.220</td>
<td>39.309</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>1.600±0.018</td>
<td>36.900</td>
<td>3.354</td>
<td>59.385</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>2.021±0.017</td>
<td>44.069</td>
<td>4.006</td>
<td>70.922</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1: In-vitro permeation pattern of optimized aceclofenac patches

Table-2: In vitro permeation of aceclofenac patch (P4) with permeation enhancer (2% Brij 58).

Fig. 1: In-vitro permeation pattern of optimized aceclofenac patches

CONCLUSION:
Transdermal Delivery of aceclofenac was thus possible from the patch formulation with the aid of surfactant Brij-58 as penetration enhancer.

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