INTRODUCTION

For topical treatment of dermatological disease as well as skin care, a wide variety of vehicles ranging from solids to semisolids and liquid preparations is available to clinicians and patients. Within the major group of semisolids preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations [1]. Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. Topical gel preparations are intended for skin application or to other mucosal surfaces for local action or percutaneous penetration of medicament or for their emollient or protective action. The physicians have a wide choice for treatment from solid dosage to semisolid dosage form and to liquid dosage formulation. Among the topical [2] formulation clear transparent gels have widely accepted in both cosmetics and pharmaceuticals. The word gel is derived from gelatin. The term gel was introduced in the late 1800 as chemists attempted to classify semisolid substances according to their physiological characteristics rather than molecular composition. Gels are semisolid systems in which a liquid phase is constrained within a three dimensional polymeric matrix of natural or synthetic gums in which a high degree of physical or chemical cross linking has been established. The USP defines gels as a semisolid system consisting of dispersion made up of either small inorganic particle or large organic molecule enclosing and interpenetrated by liquid. The inorganic particles form a three-dimensional ‘house of cards’ structure. Gels consist of two phase system in which inorganic particles are not dissolved but merely dispersed throughout the continuous phase and large organic particles are dissolved in the continuous phase, randomly coiled in the flexible chains. These chains are entangled with each other and shown as a single phase. The interaction between the colloidal phase, (inorganic or organic) set up the ‘structural viscosity’. A gel [3,4] is colloid that is typically 99% wt liquid, which is immobilized by surface tension between it and a macromolecular network of fibers built from a small amount of a gelating substance present. Gels are typically formed from a liquid phase that has been thickened with other components. The continuous liquid phase allows free diffusion of molecules through the polymers scaffold and hence release should be equivalent to that from a simple solution.

The chief disadvantage of oral NSAID’s administration is not the insufficient bioavailability [5] but rather the serious side effects of the drug. These adverse effects are mainly due to poor agent specificity, resulting from the drug binding to certain (e.g., prostaglandins) receptors. The primary site of such adverse action is the gastrointestinal tract. Orally administered NSAID’S are therefore poorly tolerated and causes stomach ulcerations. It would be desirable[6] to reach the therapeutic drug concentration in the target tissue while simultaneously keeping the systemic and gastrointestinal agent concentrations as low as possible. Obviously, such a goal can only be achieved by delivering NSAID’S into the body via the route other than the mouth. Diclofenac sodium (DS) is a nonsteroidal anti – inflammatory drug (NSAIDs) widely used clinically to reduce inflammation and pain in conditions such as rheumatoid arthritis, menstrual pain, dysmenorrhea, fever, osteoarthritis or acute injury. It has a short half-life in plasma (2 hrs) and only 50% of the drug reaches the circulation. Oral dose of diclofenac potassium causes an increased risk of serious gastrointestinal adverse events including bleeding [7], ulceration and perforation of the stomach or the intestines which could be fatal. Transdermal delivery of the drug can improve its bioactivity with reduction of the side effects and enhance the therapeutic efficacy.

In present work, attempt was made to formulate and evaluate topical hydrogel drug delivery systems. Attempts were made to enhance drug absorption and exposure to improve therapy by controlling the rate of drug release from dosage forms. Rate of drug release was modified using cross-linking agents, gelling or thickening agents. The ultimate aim was to improve bioavailability of the drug and to improve the market formulation by the use of combination of hydrophilic polymers.

MATERIALS AND METHODS

Materials

Diclofenac sodium was procured from Blue Cross (India), Carbopol 940 (Loba Chemie Pvt. Ltd., Mumbai, India), Triethaloamine (Alpha Chemika, Maharashtra, India), sodium hydroxide (Prime laboratories, Hyderabad), potassium dihydrogen phosphate (Alpha Chemika, Maharashtra, India), PEG-400 (SD
Fine Chemicals, Mumbai) were procured and used in this investigation.

**Formulation of gel**

Required quantity of carbopol was agitated in water until uniformly dispersed. Agitation was continued further for about 20 minutes. Then PEG-400 was added to the gel. Finally the gel was neutralized by adding triethanolamine in water. The drug was dispersed in small amount of water and mixed in the gel.

**TABLE 1 FORMULA FOR DICLOFENAC GEL**

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug (mg)</td>
<td>500</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td>Carbopol 940 (mg)</td>
<td>0.8</td>
<td>0.25</td>
<td>0.5</td>
</tr>
<tr>
<td>PEG 400 (ml)</td>
<td>1.25</td>
<td>2.5</td>
<td>5</td>
</tr>
<tr>
<td>Triethanolamine (mg)</td>
<td>0.25</td>
<td>0.25</td>
<td>0.25</td>
</tr>
<tr>
<td>Water (ml)</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>

**EVALUATION OF PREPARED GEL**

**Physical evaluation**

All the formulations of diclofenac sodium were evaluated for organoleptic characteristics, occlusiveness and washability.

**Homogeneity**

All developed gels were tested for homogeneity [8] by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates. Also, the homogeneity can be detected when a small quantity of the gel is rubbed on the skin of the back of the hand.

**Viscosity** [9]

The measurement of viscosity of the prepared gels was done with a NDJ-1 viscometer. The gels were rotated at 40 rpm using spindle no. 95. At each speed, the corresponding dial reading was noted.

**Spread ability**

Spread ability [10] of formulations was determined by an apparatus suggested by Multimer et al. which was fabricated in laboratory and used for study. The apparatus consists of a wooden block, with a fixed glass slide and movable glass slide with one end tied to weight pan rolled on the pulley, which was in horizontal level with fixed slide. An excess of gel sample 2.5 g was placed between two glass slides and a 100g weight was placed on slides for 5 minutes to compress the sample to a uniform thickness. Weight (60g) was added to the pan. The time (seconds) required to separate the two slides was taken as a measure of spread ability.

It was calculated using the formula,

\[ S = \frac{m.l}{t} \]

Where, S - Spreadability in g.cm / sec
m - Weight tied to upper slide
l - Length of glass slide
   t - Time in seconds

**RESULT AND DISCUSSION**

**Characterization of formulations**

The prepared formulations shared a smooth and homogeneous appearance. The diclofenac sodium gels were transparent. All preparations were easily spreadable, with acceptable bioadhesion and fair mechanical properties. At table 2 are shown the values of pH, viscosity and drug content for each gel. The pH values ranged from 7.02 ± 0.16 to 8.05 ± 0.13 which are considered acceptable to avoid the risk of irritation after skin application. Viscosity is an important physical property of topical formulations, which affects the rate of drug release; in general, an increase of the viscosity vehicles would cause a more rigid structure with a consequent decrease of the rate of drug release. The psychorheological characterization like colour, clogging, sudden viscosity change and feel of organogels are depicted in Table 2.

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Visual appearance</th>
<th>Homogeneity</th>
<th>Viscosity (cps)</th>
<th>Spread ability (g.cm./sec.)</th>
<th>pH</th>
<th>Drug content</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>Thick, translucent</td>
<td>+++</td>
<td>7131 ± 1.46</td>
<td>45.7</td>
<td>7.02 ± 0.16</td>
<td>96.91±0.87</td>
</tr>
<tr>
<td>F2</td>
<td>Thick, translucent</td>
<td>+++</td>
<td>8636 ± 1.52</td>
<td>55.9</td>
<td>7.87 ± 0.12</td>
<td>98.98±0.96</td>
</tr>
<tr>
<td>F3</td>
<td>Thick, translucent</td>
<td>+++</td>
<td>9018 ± 1.61</td>
<td>66.7</td>
<td>8.05 ± 0.13</td>
<td>99.99±0.83</td>
</tr>
</tbody>
</table>

**In vitro diffusion study**

In vitro diffusion studies were performed in phosphate buffer pH 7.4 containing SLS on the above promising formulation F3 gives maximum amount of drug release comparing to other formulations. The percentage of cumulative drug release (%CDR) of F3 is best giving 94.86% at the end of 50 mins. F1 failed the test for in vitro diffusion study showing 78.96 % drug release at the end of 50 mins and the drug release of F2 was less compared to optimized formulation. The in vitro diffusion study profiles of the above formulations are depicted in figure no.2

**Stability studies**

From freeze-thaw and thermal cycling test it was concluded that there was no phase separation observed in all the batches of diclofenac sodium formulations. The stability study of optimized formulation F3 was stored in 40° C ± 2° C at 75 ± 5 % RH for three
months. The variations of drug content, viscosity, spread ability and %CDR were within the limit which was depicted in Table 3.

Fig.2: Comparative %CDR of DS organogel formulations from batches F1 to F3.

Table 3: Stability Study of optimized formulation F3

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Initial</th>
<th>30 days</th>
<th>60 days</th>
<th>90 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual appearance</td>
<td>Thick, translucent</td>
<td>Thick, translucent</td>
<td>Thick, translucent</td>
<td>Thick, translucent</td>
</tr>
<tr>
<td>Drug content (%)</td>
<td>99.95±0.83</td>
<td>99.95±0.76</td>
<td>99.14±0.63</td>
<td>99.95±0.55</td>
</tr>
<tr>
<td>Viscosity</td>
<td>9016±1.61</td>
<td>9016±1.61</td>
<td>8099±1.67</td>
<td>8097±1.68</td>
</tr>
<tr>
<td>Spread ability (g.cm/sec)</td>
<td>66.6</td>
<td>66.6</td>
<td>66.53</td>
<td>66.48</td>
</tr>
<tr>
<td>pH</td>
<td>8.05±0.13</td>
<td>8.05±0.16</td>
<td>8.16±0.13</td>
<td>8.32±0.24</td>
</tr>
<tr>
<td>%CDR</td>
<td>94.86±0.26</td>
<td>94.16±0.28</td>
<td>94.01±0.11</td>
<td>93.99±0.29</td>
</tr>
</tbody>
</table>

CONCLUSION

It can be conclude that diclofenac sodium gel formulations prepared with gelling agent carbopol 940 showed acceptable physical properties and drug release study. All prepared gel showed acceptable physical properties concerning color, homogeneity, consistency, spread ability and pH value. The optimized formulation F3 gel formulation showed good homogeneity, good stability and drug release study. Hence the optimized formulation was found to be suitable for topical application based upon its evaluation parameters

REFERENCES


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