Chapter 7

Formulation and Evaluation of a Gel
7.1 Introduction

Extensive vehicles for dermatological diseases in different form are easily available in the market. Gels are frequently used in cosmetic and topical formulation \cite{1, 2}. Ease of application and excellent percutaneous absorption make the gels utilization more extensive in contrast to other semisolid preparations. Transparency and the stable texture of the gel are basically dependent on the selection and the conformation of the polymer used in it \cite{3}. The network formed by the polymer and coiling which is due to its self assimilation potential in the water makes the gel texture more stable under different temperature conditions. Polymer concentration in gel controls the water absorption which further helps in resisting physiological stress bears by the skin \cite{4-7}. It is well known that the prevalence of topical microbial infections are more common in comparison to systemic infection. So, finally topical agents are more preferred because of their direct and long lasting application to the skin whereas precautions are taken while selecting dermatological agents for the areas like scalp. Here different grades of polymers polymers HPMC and HPC, Carbopol 934, Carbopol 971 and Methocel were utilized to develop topical gel for localized drug delivery system of Drug.

7.2 Aim of study
The aim of this study was to evaluate the physicochemical properties of drug from topical formulation which were prepared using different polymers.

7.3 Preparation of topical gel formulations

Different grades of the synthetic and semisynthetic polymers were used as the gelling agent in the preparation of topical formulation in this study. The mixture contains different amount of ethanol and co-solvent i.e propylene glycol. Firstly, weighed amount of drug was dissolved in the ethanol and propylene glycol mixture in a 100 ml beaker containing a magnetic bar sited on a magnetic stirrer with hot plate. Additionally, to prevent evaporation of volatile component, the open end of beaker was covered with aluminium foil. Mixing speed was adjusted at 200 rpm for uniform dispersion of required amount of polymer. The mixing was done for approximately 12 hours. The gels were formed spontaneously after addition of triethanolamine in a necessary polymer to drug ratio. Partially wetted polymer lump were discarded from drug gel mixture. The formulation of gel (A-D) is shown in Tables 7.1.
Table 7.1 Formulation of Gels (A-D)

<table>
<thead>
<tr>
<th>Excipient</th>
<th>Gel A</th>
<th>Gel B</th>
<th>Gel C</th>
<th>Gel D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Carbopol 934</td>
<td>2.5%</td>
<td>------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>Carbopol 971</td>
<td>------</td>
<td>2.5%</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>HPMC+HPC (1:1)</td>
<td>------</td>
<td>------</td>
<td>2.5%</td>
<td>------</td>
</tr>
<tr>
<td>Methocel</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td>2.5%</td>
</tr>
<tr>
<td>Triethanolamine</td>
<td>1.5%</td>
<td>1.5%</td>
<td>1.5%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Propylene Glycol</td>
<td>10%</td>
<td>10%</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Peppermint oil</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Ethanol</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
</tr>
</tbody>
</table>

7.4 Physical characterization of topical gel formulations
Topical gels are intended for skin application. Gels are typically formed from a liquid phase that has been thickened with other components. The continuous liquid phase allows the free diffusion of molecule through the polymer scaffold and hence release should be equivalent to that from a simple solution. Gels were evaluated for their physicochemical properties.

7.4.1 Physical Appearance
The gels were characterized for physicochemical properties such as color, odor and consistency by visual inspection.
7.4.2 Homogeneity

When gels have been set in the container, all gels were tested for uniformity by visual inspection. Presences of any aggregates or any foreign particle were verified from this test.

7.4.3 Drug content \{8\}

Drug content was determined by dissolving accurately weighed 100 mg gels in phosphate buffer (pH 7.4). After suitable dilution absorbance was recorded by using UV spectrophotometer (Jasco 530 UV/VIS Spectrophotometer) at 245 nm. Drug content was determined using slope of standard curve, previously plotted.

7.4.4 pH \{9\}

pH-meter from systronics digital-DI-707) was used to measure pH of each topical gel. pH measurement was carried out within 24 hours of formulation of gel. Aproximately 1 gm gel was used for this study and experiment was repeated in triplicate. An average of pH was taken.

7.4.5 Drug- excipient compatibility Study \{10\}

To study the compatibility between drug and polymer of the gel was carried out on pure drug and their mixtures with polymer and other excipients on TLC plates using silica gel G. The Rf was confirmed.

7.4.7 Spreadibility \{13\}

For the determination of spreadibility excess of sample was applied in between two glass slides and was compressed to uniform thickness by placing 1000 gm weight for 5minutes. Weight (50gm) was added to the
The length of slide was 10 cm. The time required separating the two slides, i.e. the time in which the upper glass slide moves over the lower plate was taken as measure of spreadibility.

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

Where \( m \) = weight tide to upper slide
\( l \) = length moved on the glass slide
\( t \) = time taken.

7.4.8 Skin irritation test \{14\}

Rats were used for testing of skin irritation. The animals were maintained on standard animal feed and had free access to water. The animals were kept under standard conditions. Hair was shaved from skin of rats. Gel was applied (1gm) on the area of 9 cm\(^2\). The animal was observed for 7 days for any sign of edema and erythema. There is no sign of skin irritation or edema.

7.5 In vitro antimicrobial activity \{15, 16\}

Antimicrobial activity was done with the Cup plate method. Nutrient agar poured into a sterile Petridish (15 cm in diameter), and allowed to solidify. Wells were done in plate using borer of size 8mm and one gram each of formulations containing 1% of drug was poured into wells. These plates were incubated at 37±1°C for 24 hrs. The mean zone of inhibition of drug released form formulations was calculated in mm.

7.6 Stability Studies \{17\}
Formulated gel preparations were kept at different temperature condition like ambient temperature (R.T), 8±1°C (refrigerator temperature), 45±2°C at 75%±5% R.H. (condition of accelerated stability testing) for span of three months.

**7.8 Result & Discussion**

Organoleptic investigations showed that all gels are opaque and pale yellow in color with a characteristic odor of peppermint oil. Drug content of the formulations was well within the range between 88-94% and pH 6-7 (Table 7.2). Spreadibility of all gel formulations was shown in table-3 and did not produce any skin irritation. The Rf value was same as in pure compound i.e 0.67. Hence this drug is compatible with almost all polymer used in the preparation of gel.

*Table 7.2 Physicochemical properties of Gel*

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Color</th>
<th>pH</th>
<th>Homogeneity</th>
<th>Drug content (%) Mean±SD</th>
<th>Skin Irritation</th>
<th>Spreading time (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gel A</td>
<td>Yellow</td>
<td>7.6</td>
<td>Good</td>
<td>94.76±2.12</td>
<td>____</td>
<td>5</td>
</tr>
<tr>
<td>Gel B</td>
<td>Yellowish opaque</td>
<td>7.4</td>
<td>Good</td>
<td>93.51±1.46</td>
<td>____</td>
<td>6.23</td>
</tr>
<tr>
<td>Gel C</td>
<td>White</td>
<td>6.9</td>
<td>Good</td>
<td>90.89±3.59</td>
<td>____</td>
<td>120</td>
</tr>
<tr>
<td>Gel D</td>
<td>Yellowish White</td>
<td>6.8</td>
<td>Good</td>
<td>88.52±1.98</td>
<td>____</td>
<td>60</td>
</tr>
</tbody>
</table>
Table 7.3 Antimicrobial activity of different Gels

<table>
<thead>
<tr>
<th>Formulation</th>
<th>S.aureus</th>
<th>B.subtilis</th>
<th>S.dysenteriae</th>
<th>E.coli</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>24</td>
<td>25</td>
<td>25mm</td>
<td>23 mm</td>
</tr>
<tr>
<td>B</td>
<td>25</td>
<td>22</td>
<td>26</td>
<td>24mm</td>
</tr>
<tr>
<td>C</td>
<td>22</td>
<td>23</td>
<td>24</td>
<td>25mm</td>
</tr>
<tr>
<td>D</td>
<td>24</td>
<td>25</td>
<td>26</td>
<td>23mm</td>
</tr>
</tbody>
</table>

Figure 7.1 Comparison of zone of inhibition of different formulation

The antimicrobial activity of different gels is shown in Table 7.3 and all formulations show good antibacterial activity. The formulated gels were kept for stability studies. No color fading was observed for all prepared gels. The pH of all formulations were not affected and found to be in the range of 6-7. The viscosity of all gels was found to be same especially at 80°C temperature but at 45°C slight decrease in viscosity of gel. The
viscosity of Carbopol gel was found to be satisfactory for stability studies at the selected temperature.

7.9 Conclusion

Our team workers comes to conclusion that gel containing Carbopol 934 and Carbopol 971 exhibit acceptable physical properties which remained stable upon storage for 3 months at all temperature conditions.
References


