Thermoresponsive Ocular Gel Formulations of Carteolol Hydrochloride

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Introduction:
- The bioavailability of drugs delivered to the eye is often very low, typically 1% or less.
- Poloxamer 407 is a thermogelling polymer that instilled as low viscosity solutions into the eye, then the polymer changes conformation producing a gel in situ.

Objective:
To develop a poloxamer 407 based ophthalmic formulations of carteolol hydrochloride aimed at enhancing its ocular bioavailability.

Methodology:
1. Preparation of gels: Cold method.
2. In vitro release study:
   - In simulated tear fluid at 37°C and shaken at 25 rpm.
   - Samples are analysed spectrophotometrically.
3. Rheological study: Brookfield viscometer is used.
4. Stability study:
The stability of (20% poloxamer, 1% drug) is examined at 5°C, 30°C, and 40°C, at relative humidity 75%.
5. In vivo evaluation of the selected gel formulation:
The selected gel formulation is installed to the eye of albino rabbits. The drug content in aqueous humor is determined by HPLC method.

Results and Discussion:
1. Rheological study:
   - As the polymer concentration increases the number and size of micelles increase, producing a hydrophobic association and increased viscosity.
   - At 40°C there is a faster change in viscosity due to the pronounced dehydration effect of the polymer at high temperature.

Effect of storage for 16 weeks on drug release:

<table>
<thead>
<tr>
<th>Temperature</th>
<th>% Drug released at 2 hours ± SD</th>
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</thead>
<tbody>
<tr>
<td>5°C</td>
<td>38.82 ± 0.01</td>
</tr>
<tr>
<td>30°C</td>
<td>40.05 ± 0.02</td>
</tr>
<tr>
<td>40°C</td>
<td>37.81 ± 0.03</td>
</tr>
<tr>
<td>Fresh gel</td>
<td>41.76 ± 0.11</td>
</tr>
</tbody>
</table>

2. Drug release study:
   - Drug release is increased by increasing drug conc. and decreasing polymer conc.

3. In vivo study:
   - In vivo study shows that ocular bioavailability of carteolol Hcl increases by 3.6 fold for 20% poloxamer gel formulation containing 1% carteolol Hcl.

Conclusion
Poloxamer 407 formulations of carteolol Hcl shows potential for use as delivery system with improved ocular bioavailability.

References: