**Introduction:**

- Despite the accessibility of the eye, efficient delivery of drugs to treat various ocular disorders is a challenge in the field of development of ophthalmic drug delivery systems.
- Gelrite polymer originally developed as a food ingredient, and has a unique property as it is able to form viscous solutions in deionized water, which gel in the presence of cations in the tear fluids.
- Carotol is a non-selective β-adrenergic receptor blocking agent and commonly used in the treatment of glaucoma. However, it has not been marketed as an ocular in situ gel yet.

**Objective:**

The aim of this work is to develop and evaluate environmentally responsive gel (in situ gel) formulation to improve the ocular bioavailability and hence decrease the systemic absorption and side effects of carotol HCl.

**Methodology:**

1. **Preparation of gels:**
   - Gelrite of different concentrations of (0.2, 0.4 and 1%) was dispersed in deionized water, heated to 90°C while stirring until cooled to room temperature. Drug conc. was 0.5,1 and 2 μl/wk %.

2. **In vitro release study:**
   - The prepared formulation is placed in cylindrical glass containers and immersed in simulated tear fluid at 37°C and shaken at 25 rpm.
   - Samples are withdrawn at certain time intervals and analyzed spectrophotometrically at 252 nm.

3. **Rheological study:**
   - Brookfield viscometer is used.

4. **In vivo evaluation of the selected gel formulation:**
   - The selected gel formulation is installed to the eye of albino rabbits.
   - The aqueous humor is pooled at different time intervals, and the drug content in aqueous humor is determined by HPLC method.

5. **Local irritation study:**
   - It is performed by determination of blinking count after instillation of the in situ gel formulation and by observation of any redness or increased lachrymation before and after treatment.

**Results and Discussion:**

1. **Rheological study:**

   ![Figure 1. Rheogram of a) 0.2%, b) 0.4%, and c) 1% Gelrite gels prepared in STF](image)

   The flow curves of Gelrite gels indicated that at the examined polymer concentrations (0.2-1%) pseudoplastic systems were obtained. Anticlockwise hysteresis loop (thixotropy), a pseudoplastic nature characteristic, were observed in the rheogram of the Gelrite gels.

2. **Drug release study:**

   ![Figure 2. Release profiles of drug from various Gelrite formulations containing a) 0.5% b) 1% and c) 2% carotol HCI in comparison with 1% carotol HCI commercial eyedrops](image)

   Statistical analysis of the percent carotol HCI released showed that the release of drug from 0.4% and 1% Gelrite gels was significantly lower than that of commercial solution (p<0.001). The drug release kinetics from Gelrite followed Higuchi model.

3. **In vivo study:**

   A selected formulation namely, 0.4% Gelrite-1% carotol HCI was chosen to be tested in vivo and compared to commercial eyedrops, Arteoptic® 1%.

   ![Figure 3. Concentration of carotol HCI in aqueous humor after instillation of aqueous commercial solution (Arteoptic®) and 0.4% Gelrite-1% carotol HCI in situ gels](image)

   In vivo study showed that ocular bioavailability of carotol HCI measured in albino rabbits increased by 2.3 fold for 0.4% Gelrite formulation containing 1% carotol HCI compared with commercial preparation containing 1% aqueous solution.

   ![Table 1. Pharmacokinetic parameters of carotol HCI following ocular application of 25 μl of 0.4% Gelrite-1% carotol HCI formulation and commercial eye drops (Arteoptic 1%)](table)

**Conclusion:**

The developed in situ gel formulation seemed to be viable alternative to conventional eyedrops by virtue of ease of development of formulation, its good ocular tolerance and ability to enhance ocular bioavailability.

**Acknowledgement:**

The authors are grateful to the Research Center, King Saud University, Women Students-Medical Studies & Sciences Sections and to King Abdullah City for Science and Technology for the financial support.