**Formulation Optimization of Lifitegrast-Containing Ophthalmic Solution**

**Ji-Su Jeong 1**, Eun-Sol Ha1, Min-Soo Kim 1

College of Pharmacy, Pusan National University, Busan, South Korea

**Background and aims.** Lifitegrast is an anti-inflammatory agent used to treat dry eye disease. However, its susceptibility to oxidative degradation and hydrolysis presents challenges for long-term formulation stability. This study aimed to develop and optimize a stable ophthalmic formulation of lifitegrast that meets critical quality attributes under accelerated storage conditions.

**Methods.** The eyedrop formulation was designed based on the QTPP and CQAs: appearance, pH, drug content, and impurities. Excipients for buffering, pH adjustment, and osmotic regulation were included to ensure physiological suitability, and citric acid and tromethamine were selected as stabilizers. A two-factor experimental design was applied to optimize their concentrations across 20 formulations, which were stored under accelerated conditions for six months. Regression modeling and response surface analysis were used to identify the optimal design space.

**Results.** A total of 20 formulations containing varying concentrations of citric acid and tromethamine were developed to optimize the composition of lifitegrast eyedrops. After six months under accelerated conditions, all formulations exhibited acceptable appearance, pH, and drug content. Impurity levels remained below 1% in stabilized formulations, whereas the control without stabilizers exceeded the specification threshold, confirming the necessity of stabilization for long-term quality. Among the four CQAs, impurity levels varied most significantly with stabilizer concentration. Based on regression and response surface analyses, a specific range of citric acid and tromethamine concentrations was identified that consistently achieved acceptable appearance, pH, drug content, and impurity levels. The resulting design space supported robust formulation performance, with the optimal range defined as up to 2.5 mg/mL citric acid and 2.0 mg/mL tromethamine.

**Conclusion/Discussion.** A stable lifitegrast ophthalmic solution was achieved through systematic formulation design and optimization. Experimental design and statistical analysis enabled the identification of an optimal stabilizer range, ensuring long-term stability. These findings provide a practical basis for formulation advancement and future product development.

**References:**

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