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# Pharmacodynamic Evaluation of Hybrid in situ Gelling system in a Rabbit model of Bacterial Conjunctivitis

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**Abstract**

This study evaluates the pharmacodynamic efficacy of a hybrid in situ gelling system (OPT-07-1) containing Moxifloxacin for treating bacterial conjunctivitis induced by *Staphylococcus aureus* in a rabbit model. The study groups included untreated rabbits, those treated with a marketed formulation (thrice daily), and those treated with the optimized formulation (twice daily). Clinical signs—redness, inflammation, and tear score—were assessed over five days. Results showed significant improvement in the treated groups, with the optimized formulation providing comparable outcomes to the marketed product despite reduced dosing frequency. The optimized system's prolonged precorneal retention and enhanced penetration contributed to its effectiveness. These findings suggest that the hybrid in situ gel is a promising therapeutic option for ocular infections.

**Keywords:** Bacterial conjunctivitis, Pharmacodynamics, In situ gel, Hybrid formulation, *Staphylococcus aureus*, Rabbit model

## Introduction

Bacterial conjunctivitis, primarily caused by pathogens such as *Staphylococcus aureus*, remains one of the most common ocular infections globally. The condition leads to significant discomfort, including redness, irritation, and excessive tearing, and, if left untreated, can cause vision impairment. Effective treatment of bacterial conjunctivitis relies on delivering therapeutic agents directly to the infected site. However, conventional ocular formulations such as eye drops often suffer from poor bioavailability due to rapid precorneal drug loss and insufficient retention time, necessitating frequent dosing [1,2].

To address these limitations, innovative drug delivery systems such as in situ gelling formulations have emerged. These systems utilize

temperature- or pH-sensitive polymers that undergo sol-to-gel transition upon administration, prolonging drug residence time on the ocular surface. Hybrid formulations combining these polymers with lipid nanoparticles have demonstrated enhanced penetration through the corneal barrier and sustained drug release, providing a dual advantage of improved bioavailability and patient compliance [3-5].

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Such systems are particularly advantageous for treating infections like bacterial conjunctivitis, where localized, prolonged delivery of antibiotics is crucial for effective microbial eradication [6].

Several studies have evaluated in situ gels loaded with antimicrobial agents for their therapeutic effectiveness against ocular infections. For instance, formulations based on moxifloxacin, tobramycin, and lomefloxacin have shown promising results in preclinical models [7-10]. These studies highlight the potential of in situ gelling systems to enhance drug performance while reducing the dosing frequency, making them an attractive alternative to traditional eye drops.

The present study investigates a novel hybrid in situ gelling formulation (OPT-07-1) designed for the localized delivery of antibiotics to treat bacterial conjunctivitis. Using a rabbit model of bacterial keratitis induced by *S. aureus*, the pharmacodynamic efficacy of the optimized formulation was compared to a marketed eye drop formulation. Clinical outcomes, including redness, inflammation, and tear scores, were evaluated to assess the therapeutic potential of the hybrid formulation. This research aims to demonstrate the formulation's ability to provide effective treatment with reduced dosing frequency, addressing a critical need in ocular pharmacotherapy.

## Material and Method

### Animal Model

A bacterial conjunctivitis model was developed using *Staphylococcus aureus* (MTCC 96). Rabbits were divided into three groups: untreated, treated with a marketed formulation (thrice daily), and treated with the optimized formulation (twice daily).

### Evaluation Criteria

Clinical parameters—redness, inflammation, and tear scores—were graded on a scale from 0 to 5 (Table 1). Observations were made on days 0, 1, 3, and 5.

### Statistical Analysis

A t-test was used to compare data between groups, with $p<0.05$ considered statistically significant.

## Results and Discussion

### Clinical Observations

The untreated group showed progressive worsening of symptoms, with redness reaching a score of $4.17 \pm 0.41$ by day 5. Both the marketed and optimized formulations demonstrated significant improvement, with complete resolution of symptoms by day 5 (Figures 1).

### Statistical Findings

Significant differences were observed between untreated and treated groups starting from day 1 ($p<0.05$). The optimized formulation showed comparable efficacy to the marketed product (Table 2).

### Pharmacodynamic Mechanism

The hybrid formulation’s efficacy is attributed to its thermosensitive gel matrix, which provides prolonged precorneal retention, and lipid nanoparticles, which enhance drug penetration [4,6,11]. This design reduces dosing frequency, improving patient compliance while maintaining therapeutic efficacy [12-15].

**Table 1: Score index the eyes infected with *S aureus* for control group, treatment with marketed formulation and after treatment with Hybrid formulationOPT-07-1 at initial, day 1, 3 & 5th day of treatment**

| | | Day 0 | Day 1 | Day 3 | Day 5 |
|---|---|---|---|---|---|
| Redness | Untreated | 1.67 ± 0.52 | 2.67 ± 0.52 | 3.17 ± 0.41 | 4.17 ± 0.41 |
| | Marketed | 2.00 ± 0.63 | 1.83 ± 0.41 | 1.50 ± 0.55 | 0.83 ± 0.41 |
| | Test | 2.00 ± 0.63 | 1.50 ± 0.55 | 1.17 ± 0.41 | 0.33 ± 0.52 |
| Inflammation | Untreated | 1.67 ± 0.52 | 2.50 ± 0.55 | 2.67 ± 0.52 | 3.33 ± 0.52 |
| | Marketed | 1.83 ± 0.75 | 1.50 ± 0.55 | 1.33 ± 0.52 | 1.00 ± 0.63 |
| | Test | 1.83 ± 0.75 | 1.50 ± 0.55 | 1.17 ± 0.41 | 0.67 ± 0.52 |
| Tear Score | Untreated | 2.50 ± 0.55 | 3.00 ± 0.63 | 3.33 ± 0.52 | 3.67 ± 0.52 |
| | Marketed | 2.83 ± 0.75 | 2.17 ± 0.75 | 1.67 ± 0.52 | 0.83 ± 0.41 |
| | Test | 2.83 ± 0.75 | 2.00 ± 0.89 | 1.50 ± 0.55 | 0.50 ± 0.55 |

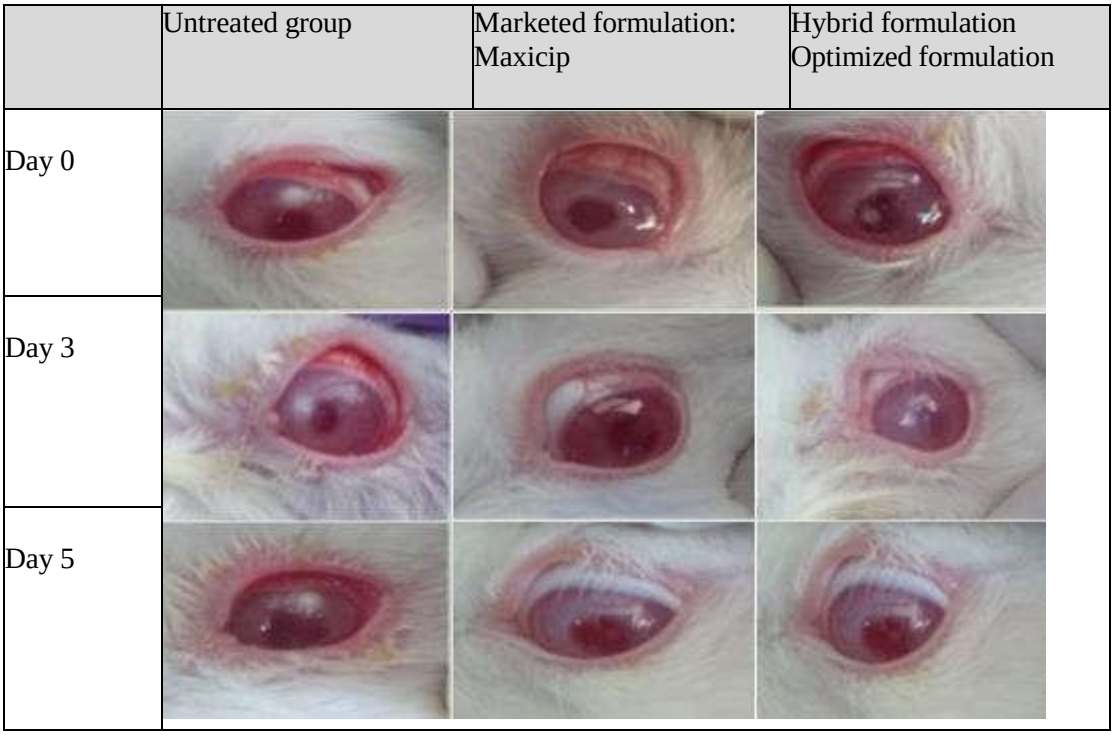


**Fig. 1: The clinical presentations of eyes infected with S aureus for control group, treatment with marketed formulation and after treatment with Hybrid formulation Optimized formulation at initial, day 3 & 5th day**

**Table 2: Statistical analysis carried out p values**

| | | | |
|---|---|---|---|
| **Test vs control** | | | |
| | **Redness** | **Inflammation** | **Tear score** |
| Day 0 | 0.3418 | 0.6655 | 0.4029 |
| Day 1 | 0.0035 | 0.0101 | 0.0522 |
| Day 3 | <0.0001 | 0.0003 | 0.0001 |
| Day 5 | <0.0001 | <0.0001 | <0.0001 |
| **Marketed vs control** | | | |
| Day 0 | 0.3418 | 0.6655 | 0.4029 |
| Day 5 | <0.0001 | <0.0001 | <0.0001 |
| **Marketed vs Inhouse** | | | |
| Day 0 | 1 | 1 | 1 |
| Day 5 | 0.0904 | 0.3418 | 0.2618 |

## Conclusion

This study successfully demonstrated the pharmacodynamic efficacy of an optimized hybrid in situ gelling formulation (OPT-07-1) for treating bacterial conjunctivitis in a rabbit model. The results showed that the optimized formulation significantly reduced clinical signs of redness, inflammation, and tearing compared to the untreated group, with therapeutic outcomes comparable to the marketed formulation (Moxicip). Notably, the optimized formulation achieved similar efficacy with reduced dosing frequency, highlighting its potential for enhanced patient compliance.

The superior performance of the optimized formulation can be attributed to its prolonged ocular retention and controlled drug release, enabled by the in-situ gel's viscosity and the lipid nanoparticles' penetration-enhancing properties. The statistical analysis further validated the formulation's effectiveness in mitigating bacterial keratitis caused by Staphylococcus aureus. By maintaining therapeutic drug levels at the infection site, the hybrid system offers a promising alternative to conventional eye drops, addressing limitations such as low bioavailability and frequent dosing.

These findings underline the potential of hybrid in situ gelling systems for ocular drug delivery, paving the way for future development of advanced formulations for treating bacterial eye infections. Further clinical studies are warranted to confirm the formulation's safety and efficacy in human subjects.

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