Improved Permeation and Retention Ocular Delivery of Cefazoline Using Thermosensitive-Mucoadhesive In Situ Gels

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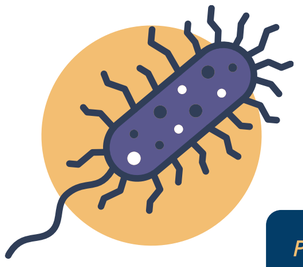
BACKGROUND



Keratitis bacteria

Pseudomonas aeruginosa

To overcome the limitations of the current route of Cefazoline eye drops.

Cefazoline was formulated into a thermosensitive-mucoadhesive in situ eye gel preparation.

In an attempt to overcome these drawbacks, alternative drug delivery system should be developed

OBJECTIVES

Developed a thermosensitive and mucoadhesive eye gel in situ containing cefazoline;
Developed a cefazoline gel in situ ophthalmic preparation with a better route of administration.

METHODS

Cefazoline (CFZ) with thermosensitive polymers pluronic F127 and F68, and hyaluronic acid as a mucoadhesive polymer.

Thermosensitive-mucoadhesive eye gel in situ

Gel in situ evaluated

- thermosensitive characteristic
- mucoadhesive characteristic
- rheological properties
- permeation and retention ability
- hemocom-patibility

RESULTS AND DISCUSSION

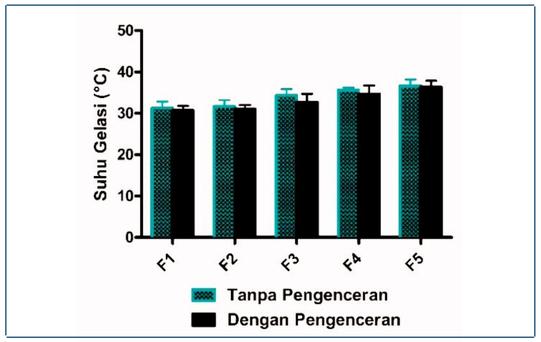


Figure 1. Mucoadhesive-Thermosensitive Gel In situ Gelation Temperature Test Results.

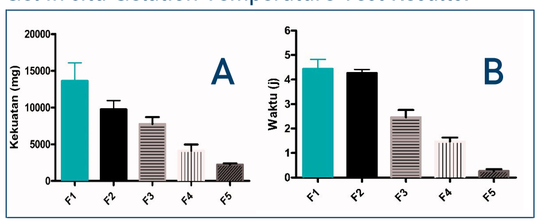


Figure 2. Mucoadhesive Gel In situ Test Results Mucoadhesive-Thermosensitive (A) Mucoadhesive Strength, (B) Mucoadhesive Time.

Essentially, the mucoadhesive strength in ocular tissue was observed to be 9748.69 ± 1184 g with more than 4 hours mocoadhesion time (Figure 2).

The optimized formulations were in situ gel containing P127, P68 and HA with the concentration of 15%, 5% and 0.2%, respectively. All formulations contained 0.35% CFZ. The optimized formulations showed gelation temperature around ocular temperature (35C), showing desired thermosensitive properties (Figure 1).

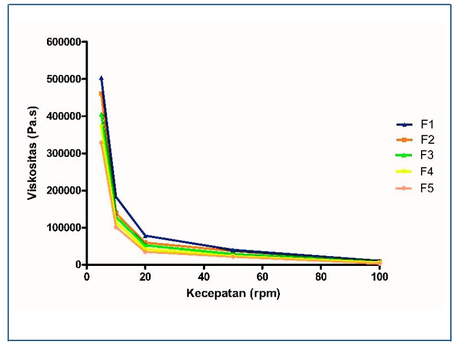


Figure 3. Ex vivo Permeation Test on Mucoadhesive-Thermosensitive In situ Gel (Mean ± SD, n = 3)

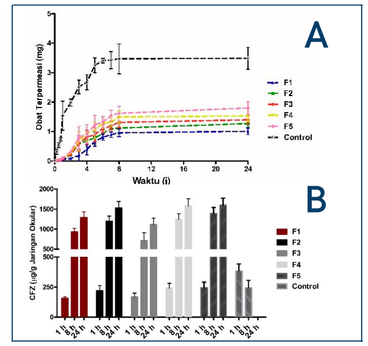


Figure 4. Result of (A) permeation and (B) retention.

The rheological evaluation showed that the in situ gel possessed desired rheological properties for thermosenstitive preparations (Figure 3). Moreover, no hemolysis was observed in hemocompatibility study. Finally, the incorporation of CFZ in this system could enhance permeation and retention of CFZ in porcine ocular tissue in ex vivo studies with 1.27 ± 0.13 mg and 1.53 ± 0.16 of CFZ permeated and localized in the ocular tissue following 24 h administration of in situ ocular gels.

CONCLUSION

Thermosensitive-mucoadhesive in situ ocular gels containing CFZ was successfully formulated. The combination of P127, P68 and HA resulted in gels with desired characteristics. Importantly, this approach improved the permeation and localization of CFZ in the ocular tissue, which could potentially improve the treatment of bacterial keratitis.

REFERENCES

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