Formulation and characterization of cubosomal in situ gel for fungal keratitis

Priya Patel*[1], Jalpa Jakhotra[1]

1. Department of Pharmaceutical Sciences, Saurashtra University, Rajkot- 360005, Gujarat

Address corresponding to

Dr. Priya Patel

Assistant Professor,

Department of Pharmaceutical Sciences,

Saurashtra University,

Rajkot-360005,Gujart, India

Email: patelpriyav@gmail.com

ABSTRACT

Objective: The purpose of the present investigation is to formulate and evaluation of cubosome loaded in situ gel for fungal keratitis.

Material and Method: The Miconazole loaded cubosomes were prepared by a top-down approach. Optimization of cubosome using box Behnken design. As formulation (independent) variables, lipid concentration (X1), poloxamer 407 concentration(X2), and homogenizer speed (X3) were used. The dependent variable was particle size (Y1), entrapment efficiency (Y2), and drug release(Y3) were investigated. 3-d surface plots and contour plots were drawn and optimized by feasibility and grid search. Identification of drug and drug-excipient compatibility study was carried out by DSC and FTIR. Particle size, PDI, and Zeta potential were analyzed by a zetatrac particle size analyzer. Entrapment efficiency, Invitro drug release study and SEM study were performed for characterization of nanoparticles. Viscosity, Gelation time and temperature, pH were performed for the characterization of nanoparticle-loaded in situ gel. An occular irritancy study was performed on a rabbit.

Result and Discussion: Cubosome was prepared by top-down method and optimized by Box-Behnken design and results show that particle size was found to be in the range of 200 to 350 nm, the entrapment efficiency was found to be in the range of 70-90%and drug release was found to be more than 80%. After preparing cubosome, that are incorporated into thermosensitive in situ gel for that carbopol 934: poloxamer 188 in the ratio of 1:20 were selected. The gelation time was found to be 41±1 second and the gelation temperature was found to be 28 ± 0.70 ºc. The checkpoint batch was formulated using the given value having predicted particle size, entrapment efficiency, and drug release respectively 209.106nm, 84.5541%, and 84.3765%, and actual (experimental) value particle size, entrapment efficiency, and drug release respectively 207.88nm, 83.79%, and 82.94%. That shows less % relative error. From the image, the surface of cubosomes can be easily studied as to whether it has a cubic shape. The drug was 90.22 % diffused after 4 hrs. study of the Franz diffusion cell. In the ocular irritancy, study results indicate that the optimized in situ gelling system was non-irritant and well tolerated by the rabbit's eyes. The antifungal activity, which was obtained by measuring the fungal growth inhibition zones, revealed that the -Cub-loaded in situ gel formulation had a 4.19-fold increase in antifungal activity compared with the MZ dispersion

Conclusion: In this study cubosome loaded in situ gel for fungal keratitis in the ocular route demonstrate that the ocular route is a promising approach and may improve the retention time of drug by the ocular route and reduce side effects related to other routes also improve patient compliance. This cubogel is an ocular dosage form to boost corneal permeability and bioavailability. The developed novel formulation is promising for the ocular delivery of a drug.

Keywords: Fungal keratitis, Ocular drug delivery, Miconazole, Cubosome, Box- Behnken design, In situ gel

References

1. Durgun ME, Kahraman E, Hacıoğlu M, Güngör S, Özsoy Y. Posaconazole micelles for ocular delivery: in vitro permeation, ocular irritation and antifungal activity studies. Drug Delivery and Translational Research. 2022;12(3):662-675
2. Thirumurthy velpandiana, jayabalan nirmala, hanuman sharmaa, sanjay sharmaa, namrata sharmab, nabanita haldera, improving therapeutic efficacy of voriconazole against fungal keratitis: thermo-sensitive in situ gels as ophthalmic drug carriers , Journal of drug delivery science and technology. 2019;49: 323-333
3. K. Morand , A.C. Bartoletti, A. Bochot, G. Barratt , M.L. Brandely , F. Chast, Liposomal amphotericin B eye drops to treat fungal keratitis: Physico-chemical and formulation stability, International Journal of Pharmaceutics,2007; 344 : 150–153.
4. Naser Tavakoli, Somayeh Taymouri, Anahita Saeidi & Vajihe Akbari, Thermosensitive hydrogel containing sertaconazole loaded nanostructured lipid carriers for potential treatment of fungal keratitis, Pharmaceutical Development and Technology, 2019: 1083-7450
5. Hoda E. Teba, islam A. Khalil & heba M. EI sorogy, Novel cubosome based system for ocular delivery of acetazolamide,drug delivery, 2021;28(1):2021-2186

6. Mahmoud A. Elfaky,alaa sirwi, heba H. Tolba, rasheed A. Shaik, nouf M. Selmi,ahlam H. Alattas,raghad S. Albreki,nuha M. Alshreef,heba A. Gad, Novel gel loaded with ketoconazole cubic liquid crystalline nanoparticles, Journal of pharmaceutical sciences. 2021; 110: 2210-2220.

7. Sinar sayed, mostafa abdel- moteleb, maha mohamed amin & omnia mohamed khowessah, Cubogel as potential platform for glaucoma management, Drug delivery 2021;28(1):293-305

8. Ribeiro A, Figueiras A, Santos D, Veiga F. Preparation and solid-state characterization of inclusion complexes formed between miconazole and methyl-beta-cyclodextrin. AAPS PharmSciTech. 2008;9(4):1102-1109.