Solid Lipid Nanoparticles for Ocular Delivery of Posaconazole: Design, Optimization and Evaluation

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Extended Abstract

Ocular drug delivery continues challenging due to the unique anatomic and physiological properties of the eye. Although the drugs are easily applied topically to the eye, different barriers such as the cornea, conjunctiva, blood-aqueous barrier, and blood-retinal barrier limit the reaching of the drugs to the target area [1]. In addition, due to some effective mechanisms such as blinking, tear turnover and drainage, the duration of the applied formulation in the eye area is very limited. For these reasons, drugs administered by the ocular route cannot reach the target area at the desired concentration and cannot remain in the ocular area for a sufficient period of time [2]. Conventional dosage forms cannot indicate enough efficacy since they are quickly removed from the eye surface by eyelid movements and tears [3]. Therefore, it is significant to design a suitable ocular drug delivery system to increase the bioavailability of drugs.

To overcome the problem of bioavailability in ocular drug delivery, it was planned to prepare solid lipid nanoparticles (SLN) systems that are using for their penetration enhancer effect in different barriers of the eye [4]. SLN are nanometer-sized particles prepared with solid lipids at room and body temperature and stabilized with emulsifiers. The use of SLN in ocular drug delivery has been increasing in recent years thanks to its advantages such as not showing toxicity problems, having high penetration ability in different barriers of the eye, increasing the ocular bioavailability and being suitable for large-scale production [5]. In addition, SLN enables autoclave sterilization, which is an important step towards the formulation of ocular preparations [6].

In the present study, posaconazole (PSZ) loaded SLN formulation was prepared and optimized to increase release and also stability. High shear homogenization and ultrasound method have been chosen as SLN preparation to prevent the use of high levels of surfactants. For the optimization of SLN formulations, response surface methodology (RSM) was used and the selected independent variables were the amounts of Compritol 888 ATO as used solid lipid and Tween 80 and Polyethylene glycol 400 as used surfactants. Encapsulation efficiency and particle size which were selected as dependent variables for SLN were found as $87.76\% \pm 2.45\%$ and 235.6 ± 4.25 nm, respectively. The zeta potential was detected as -18.2 ± 1.3 mV with a polydispersity index of 0.216 ± 0.08. The pH value of the optimized SLN formulation prepared was found to be suitable for ophthalmic application. In vitro release studies showed that the release behavior of PSZ from the optimized SLN formulations fitted well with the Higuchi kinetic model. Physical stability tests demonstrated that optimized SLN formulation was convenient for storage at $25 \pm 2°C$ for at least 60 days. As a result, optimized SLN formulation could be offered as a promising strategy for ocular drug delivery regarding their release, particle size, high encapsulation efficiency and stability.

References

[1] E. Sánchez-López, M. Espina, S. Doktorovova, E.B. Souto, M.L. García, Lipid nanoparticles (SLN, NLC): Overcoming the anatomical and physiological barriers of the eye – Part I – Barriers and determining factors in ocular delivery, Eur. J. Pharm. Biopharm, 2017.

[2] E. Sánchez-López, M. Espina, S. Doktorovova, E.B. Souto, M.L. García, Lipid nanoparticles (SLN, NLC): Overcoming the anatomical and physiological barriers of the eye – Part II - Ocular drug-loaded lipid nanoparticles, Eur. J. Pharm. Biopharm, 2017.

[3]   N.S. Punyamurthula, G.R. Adelli, W. Gul, M.A. Repka, M.A. ElSohly, S. Majumdar, Ocular Disposition of Δ8-Tetrahydrocannabinol from Various Topical Ophthalmic Formulations, AAPS PharmSciTech, 2017.

[4]   R. Cavalli, M.R. Gasco, P. Chetoni, S. Burgalassi, M.F. Saettone, Solid lipid nanoparticles (SLN) as ocular delivery system for tobramycin, Int. J. Pharm, 2002.

[5]   Z. Liu, X. Zhang, H. Wu, J. Li, L. Shu, R. Liu, L. Li, N. Li, Preparation and evaluation of solid lipid nanoparticles of baicalin for ocular drug delivery system in vitro and in vivo, Drug Dev. Ind. Pharm, 2011.

[6]   A. Seyfoddin, J. Shaw, R. Al-Kassas, Solid lipid nanoparticles for ocular drug delivery, Drug Deliv, 2010.