VORICONAZOLE-CYCLODEXTRIN COMPLEX LOADED OCULAR FILMS FOR FUNGAL KERATITIS

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Background: Fungal keratitis is one of the leading causes of ophthalmic mycosis affecting the vision due to corneal scarring. Voriconazole (VRC) is the most preferred azole antifungal agent for treating ocular mycotic infections. Shorter residence time with topical eye drops necessitate the frequent dosing (for every hour) and is associated with several drawbacks such as nasolacrimal drainage, reflex blinking accounting for < 5%bioavailability of topically applied eye drops. Apart from low aqueous solubility, VRC also suffers from stability issues. Complexation of poorly water soluble pharmaceuticals with cyclodextrin (CD) derivatives has shown to increase the solubility and stability of the therapeutic molecules.

Methods: VRC-CD complex was prepared using lyophilization technique. VRC-CD complex loaded ocular films were prepared by the solvent casting method. In vitro release study of the films was carried out using Franz diffusion cells. Ex vivo transcorneal permeation studies were performed using goat eyeball. The antifungal efficacy was carried out on *Aspergillus fumigatus*.

Results: Phase solubility suggested ~17 fold improvement in VRC solubility whereas physiochemical characterization suggested the inclusion of VRC in the cyclodextrin inner cavity. Complex loaded ocular PVA films showed the sustained release of VRC from the films and improved transcorneal permeation by several folds. The developed films demonstrated improved antifungal activity against Aspergillus fumigatus.

Conclusions: The VRC-CD loaded ocular films is a promising delivery approach for providing controlled drug release targeting the ocular tissue and served as an effective treatment regime for fungal keratitis.