

Discovery of new drug efflux transporters in human cornea - prominence in ocular drug delivery and decreased blindness

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Anterior segment ocular drug delivery typically has topical administration of ophthalmic formulations such as solutions and suspensions (Eye drops and ointments). Cornea is regarded as a primary barrier for anterior segment. Poor bioavailability of drugs administered topically to the cornea is mainly attributed to lipophilicity and tight junctions. Ocular bioavailability is ~1-10 % for topically administered drugs. Recent discovery of prominent drug efflux transporters such as MRPs1-7, P-gp, BCRP and LRP on human cornea warranted a comprehensive investigation on the role of efflux transporters in decreased ocular bioavailability. In-vitro and In-vivo screening studies demonstrated that the efflux transporters decrease the corneal permeability of glaucoma treating drugs (Bimatoprost, Latanoprost), anti-viral drugs (Acyclovir, Ganciclovir), antibiotics (Erythromycin) and steroids (Dexamethasone). In-vivo functional expression studies revealed a significant increase in aqueous humor concentrations of the drugs with the suppression of the MRP class of transporters. In light of these new findings, it was evident that a wide array of MRP efflux transporters along with Pgp and BCRP might result in poor permeation of drugs across cornea. Research should be performed to screen current ocular drugs for substrate specificity to the MRP class of transporters. Substrate specificity for each MRP homologue was found to vary significantly, though there is a common overlap. Further, localization on human corneal epithelium of the several MRP homologues, Pgp and BCRP needs to be established. Further research on the roles of individual transporters in drug resistance would benefit by knowing cellular localization.

Biography

Pradeep K. Karla, obtained his Ph.D. from University of Missouri at Kansas City in 2008. Dr. Karla is currently working as an Assistant Professor, Department of Pharmaceutical Sciences, College of Pharmacy, Howard University. Dr. Karla's discovery of new drug efflux transporters on the human ocular tissues and their role in decreased ocular bioavailability of prominent ocular drugs is cited as one of the eight prominent research discoveries that can lead to a therapeutic cure by American Association of Colleges of Pharmacy in 2009. Dr. Karla published in reputed research journals and prominent books like Adlers Physiology, Encyclopedia of the Eye etc. Dr. Karla currently serves as a Chief Editor – Pharmaceutical Sciences for the Journal, Chronicles of Young Scientists and is serving on the editorial board of multiple journals.

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