Austin Journal of Nanomedicine & Nanotechnology

Austin Publishing Group

Open Access Full Text Article

Editorial

Recent Developments in Ocular Nanotherapy

Kislay Royand Jagat R Kanwar*

Nanomedicine-Laboratory of Immunology and Molecular Biomedical Research, Deakin University, Australia

***Corresponding author:** Kislay Royand Jagat R Kanwar, Nanomedicine-Laboratory of Immunology and Molecular Biomedical Research, Deakin University, Waurn Ponds, Victoria 3217, Australia, Tel: 613-52271148; Email: jagat.kanwar@deakin.edu.au

Received: April 15, 2014; Accepted: April 16, 2014; Published: April 17, 2014

Editorial

There are 285 million visually impaired people in the world out of which, 39 million are blind. The leading causes of blindness are cataract, glaucoma, age-related macular degeneration (AMD), corneal opacities, diabetic retinopathy and trachoma. Cataract (opacification of lens) alone is responsible for 51% of total blindness [1]. Although modern cataract surgery is safe and effective, a majority of world population cannot afford it [2]. Most alternative anti-cataract synthetic drugs have failed in clinical trials due to massive side effects [3]. Current Nanotherapy approaches have gained fair bit of success in both synthetic approaches (Quercitrin) [4] and natural therapy (Curcumin) [5].

Glaucoma is the second most leading cause of blindness [6]. It is a progressive optic neuropathy and has been commonly associated with elevated intraocular pressure (IOP) [7]. Conventional drug delivery system for treatment of glaucoma comprises of ocular drops and has been linked with numerous disadvantages such as: natural anatomical barrier (low residence time), poor patient compliance, local and systemic side effects [8]. Several sustained release drug delivery systems for anti-glaucoma drugs have been proposed that include intraocular implants [9], ophthalmic inserts [10], nano-and microparticles [11], liposomes [12], nanoemulsions [13] and contact lenses [14]. However, due to potential benefits of nanoparticles (NPs) over other delivery systems further research is focussed on finding new drugs and developing better nanoformulations. One such study introduced latanoprost (an ester prodrug of prostaglandin F_{2a} with an efficiency to lower the IOP. Latanoprost acid (LA) is the pharmacologically active component of latanoprost. LA was entrapped in biocompatible and biodegradable nanoparticles formed using poly (lactide-poly(ethylene glycol) (PLA-PEGF) copolymers. The in vivo studies revealed that LA loaded NPs proved to be a promising system for curing glaucoma without inducing any side effects [15].

Topical drug delivery is considered as the easiest method for ophthalmic drug delivery and has gained patient compliance over the period of time. Once a drug is topically applied, due to the natural tear drainage and blinking action of the eye there is a 10 fold reduction in drug concentration in eye within 4-20 minutes [16]. Thus the residence time of the drug in precorneal space and penetration to ocular tissue is reduced to 5-6 minutes and 1% to 3% respectively [17]. The mucoadhesive nanoparticles that interact with the mucosal layer of cornea have been a big success in ophthalmic drug delivery, as they can increase the drug residence time in precorneal space up to 20 minutes [18]. The best advantage of using NPs is that their surface can be modified as per requirement. Thus, surface modifications in Nps can significantly increase the bioavailability, corneal penetration and conjunctival uptake of drug loaded NPs [19]. It has also been established that due to the above mentioned reasons the therapeutic efficacy of drugs loaded in polymeric NPs is significantly increased [20]. Eudragit S, methyl methacrylate methacrylic acid and chitosan are some of the mucoadhesive polysaccharides that can prolong their presence on the ocular surface [21].

Chitosan is known to increase transepithelial absorption by reversal opening of tight junctions [22]. Poly-β amino ester (PbAE) is a biodegradable and biocompatible cationic polymer that is recently being used for nanoparticle synthesis for ophthalmic drug delivery [23]. Another new mucoadhesive polymer Durasite (cross linked, poly acryclic acid, Inspire pharmaceeuticals, Durham, NC) has been designed to increase the drug residence time in precorneal space in order to improve the effect of topical delivery [24]. There have been several limitations associated with the use of nanoformulations such as, mucoadhesive polymers in solution get hydrated and their mucoadhesivity is reduced [25], other non-mucoadhesive polymers are not retained on eye for significant period therefore alternative drug delivery approaches such as nano-gels have been developed. Levofloxacin nanoparticle laden in situ gel is one such system that has been used to enhance ocular retention [26]. Other studies are focussed on improving the properties of mucoadhesive polymers by mixing other polymers eg. Cationic chitosan and anionic dextran sulphate have been used to form mucoadhesive chitosan-dextran sulphate nanoparticles with enhanced retention capability [27]. Aptamers (functional nucleic acid ligands) with enhanced specificity towards the target antigen are the current and advanced therapeutics that have been commonly used innanodelivery systems in cancer, eye and inflammatory diseases [28]. Chimerization of aptamers enhances their capability by diversifying their use in targeted therapy [29]. In a recent approach an epithelial cell adhesion molecule (EpCAM) aptamer (EpDT3)-doxorubicin (Dox) conjugate was used to target cancer stem cells using retinoblastoma (RB) cell line as a model [30]. RB is most common cancer found in the retina of children under the age of 2-3 years [31]. It was found that the EpDT-3-Dox conjugate selectively induced apoptosis in cancer as well as cancer stem cells and did not harm the non-cancerous cells. Apart from aptamers other nucleic acid based therapeutics such as RNA interference (RNAi) approach has also gained huge success in inhibiting invasiveness of RB cells [32].Therefore, the current therapeutic approach has shifted from conventional nanoparticle based therapy to highly targeted aptamers, mucoadhesive polymer mixtures, nano-emulsions and nano-gels.

Citation: Kanwar KRJR. Recent Developments in Ocular Nanotherapy. Austin J Nanomed Nanotechnol. 2014;2(3): 1018.

References

1. Pascolini D, Mariotti SP. Global estimates of visual impairment: 2010. Br J Ophthalmol. 2012; 96: 614-618.
2. Chan E, Mahroo OA, Spalton DJ. Complications of cataract surgery. Clin Exp Optom. 2010; 93: 379-389.
3. Toh T, Morton J, Coxon J, Elder MJ. Medical treatment of cataract. Clin Experiment Ophthalmol. 2007; 35: 664-671.
4. Kumari A, Yadav SK, Pakade YB, Kumar V, Singh B, Chaudhary A, et al. Nanoencapsulation and characterization of Albizia chinensis isolated antioxidant quercitrin on PLA nanoparticles. Colloids Surf B Biointerfaces. 2011; 82: 224-232.
5. Haase SC, Chung KC. An evidence-based approach to treating thumb carpometacarpal joint arthritis. Plast Reconstr Surg. 2011; 127: 918-925.
6. Blomdahl S, Calissendorff BM, Tengroth B, Wallin O. Blindness in glaucoma patients. Acta Ophthalmol Scand. 1997; 75: 589-591.
7. Coleman AL, Miglior S. Risk factors for glaucoma onset and progression. Surv Ophthalmol. 2008; 53 Suppl1: S3-10.
8. Gaudana R, Ananthula HK, Parenky A, Mitra AK. Ocular drug delivery. AAPS J. 2010; 12: 348-360.
9. Hacker MC, Haesslein A, Ueda H, Foster WJ, Garcia CA, Ammon DM. Biodegradable fumarate-based drug-delivery systems for ophthalmic applications. J Biomed Mater Res A. 2009; 88: 976-989.
10. Chetoni P, Mariotti Bianchi L, Giannaccini B, Saettone MF, Conte U, Sangalli ME. Ocular mini-tablets for controlled release of timolol: evaluation in rabbits. J Ocul Pharmacol Ther. 1996; 12: 245-252.
11. Attama AA, Reichl S, Müller-Goymann CC. Sustained release and permeation of timolol from surface-modified solid lipid nanoparticles through bioengineered human cornea. Curr. Eye Res. 2009; 34: 698e705
12. Natarajan JV, Chattopadhyay S, Ang M, Darwitan A, Foo S, Zhen M, et al. Sustained release of an anti-glaucoma drug: demonstration of efficacy of a liposomal formulation in the rabbit eye. PLoS One. 2011; 6: e24513.
13. Ammar HO, Salama HA, Ghorab M, Mahmoud AA. Nanoemulsion as a potential ophthalmic delivery system for dorzolamide hydrochloride. AAPS PharmSciTech. 2009; 10: 808-819.
14. Alvarez-Lorenzo C, Hiratani H, Gómez-Amoza JL, Martínez-Pacheco R, Souto C, Concheiro A. Soft contact lenses capable of sustained delivery of timolol. J Pharm Sci. 2002; 91: 2182-2192.
15. Giarmoukakis A, Labiris G, Sideroudi H, Tsimali Z, Koutsospyrou N, Avgoustakis K, et al. Biodegradable nanoparticles for controlled subconjunctival delivery of latanoprost acid: in vitro and in vivo evaluation. Preliminary results. Exp Eye Res. 2013; 112: 29-36.
16. Maurice DM. Kinetics of topical applied drugs. Saettone MS, Bucci P, Speiser P, editors. In: Ophthalmic drug delivery, biopharmaceutical, technological and clinical aspects. Fidia Research Series. Padova, Italy: Liviana Press. 1987; 11: 19–26.
17. Prausnitz MR, Noonan JS. Permeability of cornea, sclera, and conjunctiva: a literature analysis for drug delivery to the eye. J Pharm Sci. 1998; 87: 1479-1488.
18. Ludwig A. The use of mucoadhesive polymers in ocular drug delivery. Adv Drug Deliv Rev. 2005; 57: 1595-1639.
19. Calvo P, Sanchez A, Martinez J, Lopez MI, Calonge M, Pastor JC, et al. Polyester nanocapsules as new topical ocular delivery systems for cyclosporin A. Pharm Res. 1996; 13: 311-315.
20. Alonso MJ. Nanomedicines for overcoming biological barriers. Biomed Pharmacother. 2004; 58: 168-172.
21. Nagarwal RC, Kant S, Singh PN, Maiti P, Pandit JK. Polymeric nanoparticulate system: a potential approach for ocular drug delivery. J Control Release. 2009; 136: 2-13.
22. Felt O, Furrer P, Mayer JM, Plazonnet B, Buri P, Gurny R. Topical use of chitosan in ophthalmology: tolerance assessment and evaluation of precorneal retention. Int J Pharm. 1999; 180: 185-193.
23. Sabzevari A, Adibkia K, Hashemi H, De Geest BG, Mohsenzadeh N, Atyabi F, et al. Improved anti-inflammatory effects in rabbit eye model using biodegradable poly beta-amino ester nanoparticles of triamcinolone acetonide. Invest Ophthalmol Vis Sci. 2013; 54: 5520-5526.
24. Kuno N, Fujii S. Recent advances in ocular drug deliverysystems. Polymers. 2011; 3: 193–221.
25. Ludwig A. The use of mucoadhesive polymers in ocular drug delivery. Adv Drug Deliv Rev. 2005; 57: 1595-1639.
26. Gupta H, Aqil M, Khar RK, Ali A, Bhatnagar A, Mittal G. Nanoparticles laden in situ gel of levofloxacin for enhanced ocular retention. Drug Deliv. 2013; 20: 306-309.
27. Chaiyasan W, Srinivas SP, Tiyaboonchai W. Mucoadhesive chitosan-dextran sulfate nanoparticles for sustained drug delivery to the ocular surface. J Ocul Pharmacol Ther. 2013; 29: 200-207.
28. Kanwar JR, Mohan RR, Kanwar RK, Roy K, Bawa R. Applications of aptamers in nanodelivery systems in cancer, eye and inflammatory diseases. Nanomedicine (Lond). 2010; 5: 1435-1445.
29. Kanwar JR, Roy K, Kanwar RK. Chimeric aptamers in cancer cell-targeted drug delivery. Crit Rev Biochem Mol Biol. 2011; 46: 459-477.
30. Subramanian N, Raghunathan V, Kanwar JR, Kanwar RK, Elchuri SV, Khetan V, et al. Target-specific delivery of doxorubicin to retinoblastoma using epithelial cell adhesion molecule aptamer. Mol Vis. 2012; 18: 2783-2795.
31. McLean IW, Burnier MN, Zimmerman LE, Jakobiec FA. Tumors of the retina. In: Tumors of the Eye and Ocular Adnexa. Washington, DC: Armed Forces Institute of Pathology; 1994: 97–149
32. Subramanian N, Navaneethakrishnan S, Biswas J, Kanwar RK, Kanwar JR, Krishnakumar S. RNAi mediated Tiam1 gene knockdown inhibits invasion of retinoblastoma. PLoS One. 2013; 8: e70422.

Austin J Nanomed Nanotechnol - Volume 2 Issue 3 - 2014
ISSN : 2381-8956 | www.austinpublishinggroup.com

Citation: Kanwar KRJR. Recent Developments in Ocular Nanotherapy. Austin J Nanomed Nanotechnol. 2014;2(3): 1018.