NANOPARTICLES: NEW STRATEGIES FOR OCULAR DRUG DELIVERY

There has been a lot of activity and progress in the development and approval of new therapies for eye diseases in the past few years. Five of the 178 new drugs approved between October 2019 and December 2020 targeted eye diseases, and 2 lens-based devices were also approved in the same time frame[1]. Currently, there are over 1,500 interventional clinical trials for various eye diseases[2] so the pace of new drug development does not appear to be slowing down.

An important aspect of drug development is drug delivery to ensure maximum bioavailability and efficacy. Various drug delivery methods are used for eye medications including eye drops, gels, ocular inserts, contact lenses and injections into specific parts of the eye[3]. However, the unique anatomy and physiology of the eye poses challenges for effective drug delivery especially to the inner eye. While topical delivery is preferred for drugs administered to the front of the eye, more invasive intravitreal injections are typically used to deliver drugs to the inner eye. Topical delivery is the least invasive method to delivery drugs as eye drops or emulsions but the tear film dilutes and washes away the drug reducing bioavailability.

Nanoparticles have several characteristics that are suitable for delivery to the eye. The small size allows movement across various barriers and tissues and therapeutic modalities can be attached to the nanoparticles for delivery to the area of interest. The path of nanoparticle movement and distribution in the eye can be controlled to some extent via the modification of the size, charge and solubility of the nanoparticles as well as the route of administration[4], so it is important to design the delivery strategy optimally for the drug. The physical and chemical characteristics of the nanoparticle should be carefully designed for optimal biodistribution and should be tested on the most relevant preclinical animal models prior to clinical testing. One example is the design of gold nanoparticles to penetrate the blood-retina barrier (BRB). Studies have shown that the nanoparticles have to be 20 nm in size to successfully penetrate the BRB as 100 nm particles are too large[5]. Tracking the nanoparticle after injection can be done using fluorescence if a dye is included in the nanoparticle or a reporter marker linked to the nanoparticle. The choice of a tracking marker should be carefully tested preclinically to ensure that the biodistribution of the nanoparticles is not impacted. Another characteristic that should be considered is controlled release where drugs can be released from the nanoparticle in response to specific stimuli such as pH or light[6]. This prevents drug leakage locally or into systemic circulation to reduce adverse events and increase bioavailability of the drug.

The administration route for nanoparticles is a critical component of successful drug delivery. The cornea is the outermost barrier for topical administration but penetration enhancers can be used to move nanoparticles past the cornea. Topical delivery of nanoparticles does allow diffusion through the eye to the retina but has several challenges – the nanoparticles have to penetrate through the cornea and choroid before reaching the retina and then passing through the BRB. However, a significant number of nanoparticles enters the systemic circulation at the BRB, so higher doses of nanoparticles are needed to meet the therapeutic threshold. Though invasive, targeted injections of nanoparticles can be used to deliver drugs to specific areas in the drug. Suspending nanoparticles in hydrogels or highly viscous polymers helps immobilize them and reduces clearance. Coating nanoparticles in polyethylenglycol (PEG) helps reduce immune clearance in vascularized regions of the eye.

Nanoparticles have a great deal of promise to deliver ocular drugs and there is active research ongoing to identify particle materials that have optimal characteristics to penetrate the various static and dynamic barriers in the eye to reach the area of interest. Continuously improving systems and devices that deliver novel drugs for various ocular diseases appears to be the path of the future which is looking very bright indeed.

References:

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