NANO-POLYMER APPLICATIONS IN OCULAR DRUG DELIVERY

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ABSTRACT

Drug delivery through nanoparticles of polymers has been gaining importance because of their target specific and controlled drug delivery properties. Similar implications of these nanopolymers have been significantly carried out in ocular drug delivery too; although very few studies have been done in human beings. The conventional ocular drug deliveries draw lots of flaws in terms of drug wastage, insufficient intraocular penetration and systemic drug side effects. In this review article we have tried to briefly highlight the various studies at different centers for finding a novel ocular drug delivery carrier.

INTRODUCTION

Nanotechnology is a multidisciplinary field, which covers a vast and diverse array of devices derived from engineering, biology, physics and chemistry. In nanotechnology, a particle is defined as a small object that behaves as a whole unit in terms of its transport and properties. It is further classified according to size: In terms of diameter, fine particles cover a range between 100 and 2500 nanometers ($1nm=10^{-9}m$), while ultrafine particles, on the other hand, are sized between 1 and 100 nanometers. Similar to ultrafine particles, nanoparticles are sized between 1 and 100 nanometers.

Nanomedicine is the use of nanometer-sized particles and systems to detect and treat diseases at the molecular level; which plays an essential role in achieving the goal of eliminating the suffering and death from dreaded disease like cancer. One of the ultimate aims of nanomedicine is to create medically useful nanodevices that can function inside the body. It is envisioned that nanodevices will be hybrids of biologic molecules and synthetic polymers. Nanomedicine in present scenario is covering the aspects of medical imaging, developing ideal drug delivery carrier, cancer detection and precise anticancer therapies, gene therapy etc. Although the drug delivery system concept is not new but the emergence of nanotechnology is likely to have a significant impact on drug delivery sector, affecting just about every route of administration from oral, topical to injectable, according to specialist market research firms. Targeting delivery of drugs to the diseased lesions is one of the major aspects of drug delivery system (DDS); which seems to be in reality after the trials by nano carriers. Polymers have been used for various medical purposes including role of a drug carrying system. And recent researches are pointing towards the development of various polymer nanocomposites. Of the different dosage forms reported, nano particles attained much importance, due to tendency to accumulate in inflamed areas of the body[1].Nano particles were first developed in 1970 and were been used as carriers for vaccine and anticancer drug. But subsequent research has been oriented towards the use of nanoparticles in oral as well as ophthalmic drug delivery [2].

Topical ocular therapy is often impaired by natural physiological defense mechanisms like blinking and increase tear turn over after drug application, and also by the barriers of pre-corneal area. Conventional topical preparations have major drawbacks like poor ocular bioavailability (only around 5% of applied drop available at the site of physiological activity), and toxicities through their systemic absorption [3, 4].

Initial trials on polymer as drug carrier-

Usually various natural and synthetic viscosifying agents (polymers) were added to the vehicle in order to increase the viscosity of the preparation which can reduce the

drainage rate and subsequently improve the therapeutic efficacy [5, 6, 7, 8].But there has been no correlation between the bioavailability of drugs in rabbits and human; which was basically due to the differences in blinking frequency and tolerance in two different species [6, 9, 10, 11, 12].

Application of synthetic polymer nanoparticles-

Synthetic polymers have also been evaluated as good drug carrier of their micro and nano particles. Polycaprolactone (PCL) is the best example. PCL is a biocompatible and biodegradable polymer and significantly hydrophobic in comparison to polyalkyl cyanoacrylate[13,14].It has been found that after instillation the PCL particles aggregate in conjunctival cul-de-sac and gradually release the drug. Taking this phenomenon into consideration a study on glaucomatous rabbits showed much more pronounced reduction in IOP after instillation of PCL nanoparticles as drug carrier compared to polyalkylcyanoacrylates [15].

Advantages of chitosan nanocomposites-

De Campos et al had compared the effect of a poly ethylene glycol versus chitosan coating on the interaction of PCL nanoparticles with ocular mucosa. The in-vivo study by them had shown that the nanoparticles entered the corneal epithelium by a trans cellular pathway and penetration rate was dependant on the coating composition. Poly ethylene glycol coating enhanced the passage of the nanocapsules across whole epithelium where as chitosan coating favored the retention in the superficial epithelium; there by dual benefit of adequate penetration and continuous release of drug [16].

De Campos et al have done another study on cyclosporine. They have studied the potential of cyclosporine loaded chitosan microspheres in rabbits. They concluded that the advantages of the system included the ability to contact intimately the corneal/conjunctival epithelium. The increase delivery to external ocular tissues without compromising inner ocular structures and systemic drug exposure and provide these target tissues with long term drug levels [17].

Nanoparticles used for sub-conjunctival and intra-vitreal injection preparations-

Poly (D, L-lactic acid) and poly (D, L-lactideco-glycolide)

Micro and nanoparticles made up of poly (D,L-Lactideco-glycolide) (PLGA) has already been investigated for control release of drugs after intra-vitreal or sub-conjunctival injections [18].

Use of nanoparticles of Albumin and Lipid-

The topical application of hydrocortisone loaded albumin particles in rabbits led to a lower tissue concentration compared to a solution, due to the strong binding of the drug to the particles. Nanoparticles retention was higher in inflamed eyes than normal rabbit eyes[19].Another experiment by Zimmer et al had shown that co administration of pilocarpine-loaded albumin nanoparticles with various bio-adhesive polymers provided an effective means to improve the miotic response as well as the IOP lowering response compared to aqueous dispersion of the nanoparticles[20].

A good observation has been quoted for solid lipid nanoparticles on corneal surface as well as in conjunctival cul-de-sac. Cavalli et al have studied the use of these solid lipid nanoparticles (SLN) as carrier for delivery of topically applied Tobramycin[21].

CONCLUSION

Though the use of polymer nanoparticles for drug deliveries especially in ocular drug delivery in its infancy stage. But the significant worldwide research will come out with more and more in vivo studies in human eyes, which will provide answers to the conventional ocular drug delivery hurdles. And the novel find of bioadhesive polymer nanoparticles is certainly going to revolutionise the whole ocular drug delivery system in near future.

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