Moxifloxacin Loaded Polymeric Nanoparticles for Sustained Ocular Drug Delivery

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ABSTRACT
Efficient drug delivery to the ocular region is a challenging goal. Only a very small amount (about 1-3%) of the dosage actually penetrates through the cornea and reaches intraocular tissues. To overcome these problems of conventional dosage forms, novel drug delivery systems like nanoparticles were designed. Moxifloxacin-loaded poly (lactic-co-glycolic acid) nanosuspension was prepared with the aim of providing sustained effect for ocular delivery for 24 hours. Nanosuspensions were prepared by nanoprecipitation method using poly(lactic-co-glycolic acid) and evaluated for particle size, surface morphology, zeta potential, drug entrapment efficiency, in vitro release and ex vivo transcorneal permeability, and were compared with marketed products. Microbiological efficacy was tested against Staphylococcus aureus and Pseudomonas aeruginosa using cup plate method.

Spherical uniform particles (202.5 nm) with a polydispersity index of 0.226 and negative zeta potential (– 25.45 mV) were obtained for MF4 (drug to polymer ratio 1:0.4). Drug entrapment efficiency for MF4 was found to be 83.1%. The cumulative percent drug release for formulation MF4 after 24 hours was 86.1%, showing a sustained effect in controlling the bacterial conjunctivitis thereby avoiding frequent administration of dosage. MFX-loaded PLGA nanoparticles (MF4) showed a significantly higher drug permeation capability compared to the commercial marketed eye drops in ex vivo transcorneal permeation studies and also showed better antimicrobial efficacy compared to the marketed formulation. The results indicate that Moxifloxacin-loaded PLGA nanosuspension could be utilized as a potential drug delivery system for sustained release in ophthalmic application.

KEYWORDS: Moxifloxacin; PLGA nanoparticles; nanoprecipitation method; ex vivo transcorneal permeation.

Introduction
Acute bacterial conjunctivitis is the most prevalent infectious condition, commonly caused by bacterial species like Streptococcus pneumoniae, Haemophilus influenza and Staphylococcus aureus. Newer-generation fluoroquinolones play a major role in the treatment of bacterial conjunctivitis because these agents act quickly against a broad spectrum of pathogens, including most of the bacteria that could be causative agents for bacterial conjunctivitis (Finkel et al., 2009).

With eyes being the most readily accessible organ in the body, achieving good ocular bioavailability is still a challenging task. The bioavailability of ocular drugs in conventional systems that are aqueous solutions is usually low because of quick elimination from the eyes due to reflex blinking and tear drainage. The corneal barrier also plays a significant role in low ocular bioavailability. Nanoparticles come out to be the most promising application in ocular drug delivery (Mandal et al., 2009). Treatment with nanoparticle systems increases bioavailability, reduces administration frequency and promotes drug targeting (Vega et al., 2008).

The most commonly used polymers for ocular nanoparticles are poly(alkyl cyanoacrylate), polycaprolactone, and poly(lactic acid)/poly(lactic-co-glycolic acid) (PLGA). These polymers are biodegradable and undergo hydrolysis in tears (Ding, 1998). Among them PLGA is the most suitable candidate for nanoparticle formation because of its ease of formulation and approval for use in drug delivery application by the Food and Drug Administration (FDA; Jain, 2000). These polymers have a long history of safe human use as a raw material for nanoparticle production of enzyme sensitive drugs (Reis et al., 2008). Poorly water soluble drugs are difficult to develop as a conventional ocular drug delivery system (Patravale VB et al., 2004). Nanotechnology can be used to formulate such poorly water soluble drugs as a nanosuspension and offers the opportunity to address many of the deficiencies associated with such class of drugs (Kassem MA et al., 2007).

Moxifloxacin, a fourth generation fluoroquinolone antibiotic shows good activity against anaerobic as well as gram-positive organisms (Darlene Miller, 2008). Moxifloxacin HCl is available in the form of drops (0.5 % w/v) for ophthalmic use and its FDA-approved dosing

ABBREVIATIONS: Moxifloxacin (MFX); poly-(lactic-co-glycolic acid) (PLGA).