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The potential of using biodegradable microspheres in retinal diseases and other intraocular pathologies

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ABSTRACT

Pathologies affecting the posterior segment of the eye are one of the major causes of blindness in developed countries and are becoming more prevalent due to the increase in society longevity. Successful therapy of diseases affecting the back of the eye requires effective concentrations of the active substance maintained during a long period of time in the intraocular target site. Treatment of vitreoretinal diseases often include repeated intravitreous injections that are associated with adverse effects. Local administration of biodegradable microspheres offers an excellent alternative to multiple administrations, as they are able to deliver the therapeutic molecule in a controlled fashion. Furthermore, injection of microparticles is performed without the need for surgical procedures. As most of the retinal diseases are multifactorial, microspheres result especially promising because they can be loaded with more than one active substance and complemented with the inclusion of additives with pharmacological properties. Personalized therapy can be easily achieved by changing the amount of administered microspheres. Contrary to non-biodegradable devices, biodegradable PLA and PLGA microspheres disappear from the site of administration after delivering the drug. Furthermore, microspheres prepared from these mentioned biomaterials are well tolerated after periocular and intravitreal injections in animals and humans. After injection, PLA and PLGA microspheres suffer aggregation behaving like an implant. Biodegradable microspheres are potential tools in regenerative medicine for retinal repair. According to the reported results, presumably a variety of microparticulate formulations for different ophthalmic therapeutic uses will be available in the clinical practice in the near future.

Contents

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1. Introduction

Pathologies affecting the posterior segment of the eye are one of the major causes of blindness in developed countries. These diseases include uveitis, diabetic retinopathy, macular edema, endophthalmitis, proliferative retinopathy, age related macular degeneration and glaucoma, among others. Generally, back of the eye diseases are chronic and degenerative and some of them are related to elderly. Successful treatments of vitreoretinal diseases require effective concentrations of the active substance maintained during long periods in the target site. Statics barriers (different corneal layers, sclera, retina, blood aqueous and blood retinal barriers), dynamic barriers (tear dilution, conjunctival and choroidal blood flow, and lymphatic clearance) as well as efflux pumps, effectively limit the drug access to the posterior segment (Gaudana et al., 2010). Four routes of administration can be theoretically employed to deliver active substances to treat retinal diseases: topical, systemic, intraocular and periocular (Herrero-Vanrell and Refojo, 2001). The poor bioavailability of topically administered drugs limits their access to intraocular tissues. Systemic administration requires high doses to achieve adequate therapeutic levels of the drug in the eye with the risk of systemic adverse effects. Intraocular local drug administration includes injections into the anterior chamber of the eye (intracameral), in the vitreous (intravitreal) or into the periocular tissues (subconjunctival, sub-Tenon, juxtascleral and retrobulbar). Due to the difficulty in the maintenance of therapeutic concentrations in the target site, repeated intraocular injections are required for a successful therapy causing much inconvenience to patients. Although the periocular route is getting more attention, intravitreal injections are still the most employed even being associated to non-desired effects. For example, if high doses of the therapeutic agent are administered the concentration in the retina can be toxic. Besides, successive intravitreal injections are related to adverse effects such as cataracts, retinal detachment, and haemorraghes, among others. Moreover, the risk of the non-desired effects increases with the number of injections (Herrero-Vanrell et al., 2000).

Drug delivery systems for the treatment of posterior segment diseases are classified into 3 major categories: (1) intraocular controlled (sustained) release by implants, (2) drug targeting for systemic administration (e.g. photodynamic therapy) and (3) drug penetration (e.g. iontophoresis) (Yasukawa et al., 2011). Innovative treatments as intraocular drug delivery systems in different sizes have been developed to provide sustained drug concentrations of the active substance in the target site. They are constituted by a combination of drugs and biomaterials. Encapsulated cell technologies have been developed also (Yasukawa et al., 2011). Depending on the properties of the biomaterial (erodible or biodegradable and non-erodible or non-biodegradable), the devices can disappear from the site of administration or remain there during the lifetime of patients.

According to their size, devices are classified as implants (>1 mm), microparticles (1–1000 μm) and nanoparticles (1–1000 nm). Considering their physical structure they are divided