Abstract

Vision impairment and blindness severely compromise the quality of life of a great part of the global population, as it was estimated that in 2015 more than 250 million people were living with moderate to severe vision impairment or blindness. Retinal diseases correspond to the leading cause of vision impairment worldwide especially in industrialized countries, and their prevalence is on the rise as a result of the rapid growth of the aging population. Development of effective treatments for retinal diseases has being a constant challenge for drug delivery scientists, since delivering therapeutically relevant concentrations of drugs at the posterior segment of the eye is compromised by the presence of structural and physiological barriers. Nanoparticle drug delivery systems have been previously incorporated in an attempt to overcome some of the limitations of the conventional ocular drug delivery strategies. Lipidic nanoparticles specifically are an interesting option due to their attractive characteristics like low cytotoxicity, high loading capacity of both hydrophobic and hydrophilic drugs, easily functionalized surface and customized characteristics.

Throughout this PhD work, we utilized lipidic nanoparticles in order to deliver therapeutic agents to the retina, in a targeted and sustained manner, for the treatment of diabetic retinopathy and dry age-related macular degeneration. In the first part of this study, we showed for the first time that endothelial protein C receptor (EPCR) is expressed by human retinal endothelial cells and that it holds promise as a target for active drug delivery to the inner blood-retinal barrier. We developed a corticosteroid loaded, EPCR targeting liposomal system that demonstrated enhanced liposomal internalization from the retinal endothelium and significantly superior therapeutic efficacy compared to non-targeting formulations. While for the second part of the thesis, we work on the development and characterization of a solid lipid nanoparticle drug delivery system, with main objective the delivery of hydrophobic, antioxidant compounds to the outer retinal barrier, for the protection of the retinal pigment epithelium (RPE) as a treatment of dry AMD.