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A new model for developing intravitreal formulations

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Damage to the posterior segments accounts for over 70% of the blind registrations in Europe. Treating many blinding conditions requires a medicine to be in the posterior cavity for a sufficient period of time. Inflammatory, angiogenic and fibrotic process in the retina causes tissue damage and vision loss. These biological processes are also major contributors to the failure of current treatments for these diseases. As the elderly segment of the population continues to grow, there is an urgent and unmet need to optimize the dose and duration of action of medicines in the posterior segment. The development of new therapeutic proteins is of particular importance since proteins tend to be fast-acting, selective and potent. New dosage forms and drug delivery systems (DDSs) are also being developed to augment the treatment of chronic blinding conditions and new DDSs are particularly needed for therapeutic proteins. During preclinical development, allometric modeling from in vivo models is not reliable due to: (i) the multitude of anatomical differences between animal and human eyes; and (ii) the immunological response of animals caused by the administration of a humanized protein. The formation of anti-drug antibodies (ADAs) in animals towards humanized proteins results in accelerated clearance rates making it impossible to evaluate prolonged dosage forms of new protein therapeutics. To prolong the release of a protein, a wide array of novel injectable formulations are being developed and reported in literature. The PK-eye in vitro model is a two-compartment, aqueous outflow model that has been shown to be particularly useful to estimate human protein PK profiles and to determine protein stability properties. Given the current design of the PK-Eye, there is now an opportunity to establish correlations with in vivo models using different injectable dosage forms. The PK-Eye model is used to evaluate new DDS and formulations that are being developed to prolong the release of a protein therapeutic. The PK-Eye is also being used to develop long- acting formulations and implants derived from non-protein low molecular weight (MW) actives. In contrast to proteins, low MW actives will generally clear by both (i) aqueous outflow and (ii) retinal permeation into the retina choroid sclera (RCS) pathway. Poorly soluble steroids are clinically used as suspensions and implants. TA (Kenalog®) displayed a residence time in the PK-Eye model that was 50% longer than what is observed in humans. Using permeation data to estimate retinal clearance pathways allow the determination of in-vitro *in-vivo* correlations (IVIVCs) during preclinical research. As a result, use of the PK-Eye can also estimate the human clearance times of long-acting implants of permeable drugs.

Biography

Sahar Awwad is a Post-doctoral Research Scientist at the University College London, School of Pharmacy, UK. She has recently completed her PhD under the supervision of Professor Steve Brocchini and Professor Sir Peng Tee Khaw. She obtained two scholarships for her PhD: (i) UCL Overseas Research Scholarship (ORS), and (ii) NIHR Biomedical Research in Ophthalmology at Moorfields Hospital. She has done her MSc in Drug Delivery from the University of London, School of Pharmacy (London, UK) and BPharm from Jamia Hamdard University (New Delhi, India). She has worked on various projects that have resulted in the development of a new in vitro model of ocular pharmaceutics along with a new strategy for extending the duration of action of therapeutic proteins in the eye. Her projects are widely based on drug delivery, ocular pharmaceutics, determination of IVIVCs for ocular PK and biodistribution properties, protein production, protein modification and protein characterization (surface plasmon resonance, stability and activity). She is the Co-founder of Optceutics Ltd., a new company utilizing the PK-Eye to develop new formulations.

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