ABSTRACT

The challenging nature of the ocular drug delivery terrain continues to drive the search for innovative platforms that will counter the challenges of delivering effective patient-friendly therapeutic solutions. For many ocular therapeutics, the challenge has been finding a means to deliver high molecular weight, poorly soluble bioactives, across the formidable barriers presented by the physio-anatomical ocular structures. This challenge is more for bioactives used to treat chronic ailments in predominantly vulnerable populations such as the elderly and the children. In addition, many ocular conditions co-exist in an individual, necessitating the need for multiple treatment plans. For such individuals, using safer delivery options with higher bioactive loading capacity is a *sine qua non.* This thesis details the design, development, characterization, and evaluation of a novel ocuterial to overcome the challenge of cytocompatibility for implantable ocular devices. Modification by bulk zwitterionization was adopted as opposed to surface modification given that surface modification is short-lived in the dynamic ocular space.

Polyvinyl alcohol (PVA) was selected as the ideal polymer framework given its ocular application history together with the bioinspired sulfobetaine methacrylate. Facile photo-initiated crosslinking polymerization (a process amenable to both moulding and 3D printing) was used to synthesize and optimize the novel hydrogel properties. *In vitro* characterization was undertaken to assess the physicochemical parameters such as water contact angle, that underscore the hydrophilicity and consequently protein resistance potential of the novel hydrogel. The mechanical strength of the novel hydrogel that delineates its ability to withstand stress that could arise from handling (with forceps during implantation or by patients for contact lens application) was also evaluated. The optimized hydrogels' crushing strength was above 21 Mpa % at 70 % strain and translates to a superior mechanical robustness for a super-hydrophilic hydrogel. Zwitterionization increased the transparency (shown by over 99 % transmittance, a perquisite for lens applications); improved equilibrium water content (directly correlates with oxygen transmissibility and permeability that is specifically important for corneal health in extended wear contact lenses); contributed to superhydrophilicity (shown by a water contact angle < 10º) and translates to a high protein resistance/antifouling potential; improved *in vitro* protein adhesion resistance (< 0.1 µg/mm^2); facilitated drug loading and *in vitro* drug release of a model hydrophobic drug molecule, cyclosporine A; and decreased biofouling potential (>87%) to *S. aureus* and *E. coli*. *In vivo* sub conjunctival

implantation of the optimized hydrogel in New Zealand albino rabbits demonstrated its low capacity to trigger pro-inflammatory responses, an absolute requirement for implantable ocular devices given the risks inflammation presents in the ocular space. These results underscore the potential for application of the novel ocular biomaterial as an intraocular sub-conjunctival implantable device that could double as a drug delivery device.