Synthesis of Zwitterionic Derivatives of Phosphorylcholine for Use in Contact Lenses and Biocompatible Coatings

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Statement of Purpose: The novel polymer biomaterials presented in this paper are prepared with inspiration from the surface layer of cell membranes.
2-(methacryloyloxyethyl)phosphorylcholine (MPC)[1] is a biocompatible monomer used as a component in coatings for various types of medical devices.[2,3] This biomaterial exhibits zwitterionic properties due to its positive and negative charges and also presents a vinyl moiety that allows for copolymerization with other vinylic monomers. Derivatives exhibiting additional functionality to that of MPC should provide enhanced properties with regards to biocompatibility and non-thrombogenicity. Thus, a 4-step synthesis was designed to form the novel derivatives.

Methods: The synthesis of phosphorylcholine derivatives involves similar steps to the ones described for the synthesis of MPC.[1] The zwitterionic entity was used dry and pure. 2-hydroxyethyl methacrylate (HEMA) and *n*-butyl methacrylate (BMA) were purified by distillation under vacuum. 2,2'-Azodi(2-methylbutyronitrile) (AMBN), ethylene glycol dimethacrylate (EGDMA) and Perkadox16 were used as received. Human platelet poor plasma was collected from human blood plasma, centrifuged and diluted.
Contact lenses were formed from a solution of 80% (w/w) HEMA with 20% (w/w) of the zwitterionic derivative and 0.2% (w/w) of EGDMA. The mixture was stirred, degassed and Perkadox16 (0.3%, w/w) was added. A few drops of this formulation were placed in polypropylene moulds, sealed and cured in the oven at 80°C for 2 hours, followed by 30 min at 100°C. The cured lenses were immersed in a solution of phosphate buffered saline to measure their water content. The hydrated lenses were then incubated in a solution of lysozyme (0.5mg/mL) for 24 hours and the adsorption was measured with a Perkin-Elmer UV/Vis spectrometer.
The zwitterionic entity was also polymerised with 80% of BMA (w/w) in methanol, using AMBN as a radical initiator. The mixture was degassed under nitrogen and the bottle was sealed. The mixture was stirred at 100°C for 1 hour, then precipitated in water. The wettability was observed via dip coating on polypropylene tubes and the platelet adhesion was assessed on coated glass plates using a microscope.

Results: The high water content HEMA lens (used as a reference) adsorbed 71.2% of lysozyme, whereas the lens made of 80% HEMA + 20% of the novel zwitterion (w/w) displayed an adsorption of 6.6%. **Table 1** shows a comparison of the water content between 4 different contact lenses.

Lenses	Water absorption
100% hydroxyethyl methacrylate (HEMA)	38%
High water content HEMA lens	68%
80% HEMA + 20% novel zwitterionic material	58%
ProClear [3] (80% HEMA + 20% MPC) Market leader	59%

Table 1: Comparison of water content of 4 different contact lenses

The zwitterion-containing contact lens demonstrated high water content comparable to that of the market leader (ProClear). This value (58%) is an improved performance compared to the commercial 100% HEMA lenses.

The polymer containing 20% of zwitterionic entity and 80% of BMA displays very good hydrophilicity. **Figure 1** shows the difference in contact angle between an uncoated polypropylene tube and a coated tube.

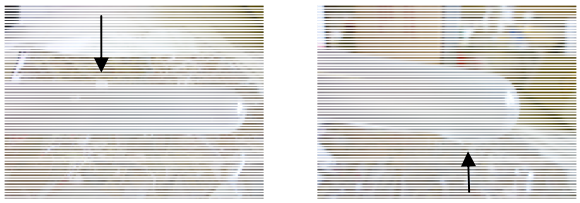

Figure 2: Comparison between an uncoated polypropylene tube (left) and a zwitterion-containing coated tube (right)

Furthermore, platelet adhesion was found to be decreased by 60% on a plate coated with the zwitterionic polymeric assembly when compared to an uncoated plate.

Conclusion: Contact lenses made with 20% of the novel zwitterionic entity provides strong resistance to tear film enzymes and high water content in comparison to the similar manufactured contact lenses (ProClear). In addition, the same zwitterionic entity engenders excellent hydrophilicity and good platelet resistance when blended with BMA. Our future work will involve the development and evaluation of further polymeric assemblies to enhance the haemocompatibility and provide a range of polymers for blood-contacting medical devices and contact lenses.

References:

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