

A Biocompatible Contact Lens to Prevent Non-Specific Protein Adsorption: Development of Novel Procedure to Modify Hydrogels with Phosphorylcholine

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Statement of Purpose:

Phosphorylcholine (PC) group existing extensively on the surface of cell membranes is well known as a biocompatible compound. PC compounds have received a lot of attentions as a biomaterial for medical equipments or cosmetics due to its interesting properties, however, most of the studies have been based on polymerized PC-monomers [1]. Whereas, we have focused on low molecular-weight PC compounds such as “Phosphorylcholine Glyceraldehyde (PCGA)” or “Carboxymethyl Phosphorylcholine (CMPC)” [2]. These reactive PC compounds are capable to modify material surface with covalent bonds. Advantages of this modification method are the high strength to connect PC with modified material, and the controllability of PC density on the surface.

In this study, the procedures and the effects of PC modification of hydrogels that will be applicable to contact lenses are reported.

Methods:

Hydrogel: Three kinds of commercially available contact lenses were used as hydrogel samples; Etafilcon A (poly-HEMA-co-MA, Vistakon), Polymacon (poly-HEMA, Bausch & Lomb), and Nelfilcon A (PVA, CIBA Vision). All lenses were rinsed with water before subsequent operation.

PC Modifying Procedure: Run 1 Etafilcon A: Etafilcon A was washed with anhydrous DMF by repetitive decantation, and immersed in anhydrous DMF (6 g). Ethylenediamine (4.8 mg, 0.08 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) (15.3 mg, 0.08 mmol), and 1-Hydroxybenzotriazole (10.8 mg, 0.08 mmol) were added at r.t., and reacted for 5 h. After washed with DMSO, the Etafilcon A, CMPC (19.3 mg, 0.08 mmol), EDC (15.3 mg, 0.08 mmol), and *N*-hydroxysuccinimide (9.2 mg, 0.08 mmol) were reacted in H₂O/DMSO 1/4 w/w (5.0 g) at r.t. for 12 h. **Run 2 Polymacon:** Polymacon was washed with anhydrous DMSO, and immersed in anhydrous DMSO (3 ml). CMPC, *N,N'*-carbonyldiimidazole (CDI), and triethylamine (TEA) were added at r.t., and reacted for 12 h. [Run 2-1 CMPC (20.5mg, 0.085 mmol), CDI (5.6mg, 0.035 mmol), TEA (8.6 mg, 0.085 mmol). Run 2-2 CMPC (41.0mg, 0.17 mmol), CDI (28.0 mg, 0.17 mmol), TEA (17.2 mg, 0.17 mmol)] **Run 3 Nelfilcon A:** Nelfilcon A was immersed in 1M HCl aq. (5.0 g) and PCGA were added and reacted at 40 °C for 2 h. [Run 3-1 PCGA (50 mg, 0.22 mmol). Run 3-2 PCGA (150 mg, 0.67 mmol)]

The amount of PC group was determined by a molybdenum-blue method [3]. Sodium dihydrogenphosphate solution was used as a reference compound.

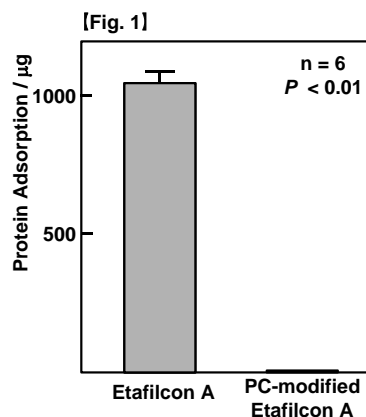
Protein Adsorption Test: Artificial tears solution (ATS) was prepared by the previous report [4]. Etafilcon A and PC-modified Etafilcon A were immersed in ATS (3 ml)

respectively, and shaken gently at r.t. for 24 h. The Lenses were rinsed with phosphate buffer solution, and proteins adsorbed on the lens were washed with 5% sodium dodecyl sulfate aqueous solution. The amount of the protein was determined by bicinchonic acid (BCA) assay (PIERCE) or micro-bicinchonic acid assay (PIERCE). Albumin (bovine serum) was used as a reference compound.

Results / Discussion:

The Amounts of PC Group modified on the hydrogels in run 1, 2-1, 2-2, 3-1, and 3-2 were 1.13 μmol, 0.32 μmol, 9.60 μmol, 0.36 μmol, and 1.07 μmol, respectively. It was confirmed that every contact lens was modified with PC group, and the amount was easily controllable by changing the amount of PC compound in the reaction.

Fig 1 shows the result of the protein adsorption test of the contact lens acquired in run 1.



The amounts of the total protein adsorption on the Etafilcon A and PC-modified Etafilcon A were 1036 ± 44 μg and 6.9 ± 1.4 μg, respectively. The PC-modified Etafilcon A was able to prevent protein adsorption quite effectively though the total amount of PC group in the whole hydrogel is small. We considered that the reason was due to the localization of PC group on the outermost surface of the hydrogel.

Conclusions:

Various PC-modifying procedures on hydrogels possessing carboxyl group or hydroxyl group were studied, and the effect to prevent non-specific protein adsorption was confirmed. This modification method possibly provides contact lenses with simple care and comfortable wearing.

References:

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