

ENHANCING HYDROPHILICITY AND PROTEIN RESISTANCE OF SILICONE HYDROGELS BY PLASMA INDUCED GRAFTING WITH HYDROPHILIC POLYMERS*

Fu-qian Sun, Xin-song Li**, Pei-ting Cao and Jin-ku Xu

Biomaterials and Drug Delivery Laboratories, School of Chemistry and Chemical Engineering, Southeast University, Nanjing 210018, China

Abstract The hydrophilicity of silicone hydrogels used as soft corneal contact lens plays an important role in wearing comfort. In order to enhance hydrophilicity and protein resistance, silicone hydrogel membranes were modified by atmospheric pressure glow discharge plasma (APGDP) induced surface graft polymerization of *N*-vinyl pyrrolidone (NVP) and poly(oligoethylene glycol methyl ether methacrylate) (PEGMA) in this paper. XPS analysis demonstrated the success of graft polymerization of NVP and PEGMA onto the surface of silicone hydrogel membranes. The hydrophilicity of silicone hydrogels was characterized by the measurement of water contact angle (WCA). The result showed that NVP grafted silicone hydrogel has the WCA of about 68° and PEGMA grafted silicone hydrogel has the lowest WCA of about 62°, while the pristine silicone hydrogel is hydrophobic with the WCA of about 103°. Protein resistance of silicone hydrogels was investigated by the method of bicinchoninic acid assay using bovine serum albumin (BSA) as a model. It's found that the grafted silicone hydrogel has a significant improvement of protein resistance, and PEGMA grafting is more efficient for the reduction of protein adsorption than NVP grafting. The silicone hydrogel membranes grafted with NVP and PEGMA are good candidates of soft corneal contact lenses.

Keywords: Silicone hydrogel; APGDP; Graft polymerization; Hydrophilicity.

INTRODUCTION

Silicone hydrogel has attracted much attention as a new generation of soft contact lens which can provide sufficient supply of oxygen to the cornea for the metabolic requirements. However, the surface of unmodified silicone hydrogels is hydrophobic. There is a need to design the surface structure and hydrophilic properties of silicone hydrogels to be compatible with the corneal epithelium environment to enhance wearing comfort and anti-deposition of protein. The improvement of surface hydrophilicity of silicone hydrogel will give a greater comfort to the wearer and additionally prevent the formation of deposits such as proteins and lipids, as well as microbial colonisation^[1, 2].

Plasma treatment is a simple and versatile method for the surface modification of biomaterials, which can improve hydrophilicity without changing bulk material properties^[3–6]. Conventional plasma treatment using various gases like oxygen and methane as medium can be applied to silicone hydrogel contact lens^[7, 8]. Grafting of hydrophilic polymers onto biomaterials is an alternative approach to improve hydrophilicity and protein resistance^[9, 10]. Hydrophilic polymers can be covalently attached to the surface of biomaterials by graft polymerization of hydrophilic monomers after initiating with ozone^[11, 12], ion sputter^[13] and plasma^[14–16].

* This work was financially supported by Hydron Contact Lens Co., Ltd and National Natural Science Foundation of China (No. 50673019).

** Corresponding author: Xin-song Li (李新松), E-mail: lixs@seu.edu.cn
Received June 8, 2009; Revised August 3, 2009; Accepted August 17, 2009
doi: 10.1007/s10118-010-9082-1

Poly(oligoethylene glycol methyl ether methacrylate) (PEGMA) and *N*-vinyl pyrrolidone (NVP) are well-known hydrophilic and biocompatible monomers, which can be grafted onto biomaterials surface to reduce protein absorption^[17, 18], inhibit platelet adhesion^[19] and suppress cell/bacteria attachment^[20, 21]. However, to our knowledge, there are until now no reports of the grafting of PEGMA and NVP onto silicone hydrogels for the development of soft contact lens with enhanced hydrophilicity and protein resistance.

In the present report, silicone hydrogels were prepared by copolymerization of methacrylated polydimethylsiloxane macromonomer, hydrophilic monomer *N,N*-dimethyl acrylamide (DMA) and hydrophobic monomer 3-methacryloxypropyl tris(trimethylsiloxy silane) (TRIS), and were further modified by atmospheric pressure glow discharge plasma (APGDP) induced graft polymerization of two hydrophilic monomers of PEGMA and NVP. The surface structural change and hydrophilicity of silicone hydrogels were characterized by X-ray photoelectron spectroscopy (XPS) and contact angle measurements. The protein resistance was evaluated by bovine serum albumin (BSA) deposition assay.

EXPERIMENTAL

Materials

Bitelechelic polydimethylsiloxanes (MA-PDMS-MA) macromonomer was synthesized with the method as described in the literature^[22] by ring opening reaction of glycidyl methacrylate (GMA, Shanghai Heshibi Chemicals, China) with amine ended polydimethylsiloxanes (KF8010, Shin-Etsu Chemicals, Japan). 3-Methacryloxypropyl tris(trimethylsiloxy silane) (TRIS) (98%) were purchased from Alfa Aesar. *N,N*-dimethyl acrylamide (DMA) and ethylene glycol dimethacrylate (EGDMA) was purchased from Shanghai Heshibi Chemicals, China. *N*-vinyl pyrrolidone (NVP) was supplied by Jiaozuo Yuanhai Fine Chemicals, China and distilled before use. Poly(oligoethylene glycol methyl ether methacrylate) (PEGMA) of average molecular weight 1000 was supplied by Taijie Chemicals, China. Photoinitiator Darocur 1173 was a CIBA product. Ammonium ferrous sulfate was supplied by Shanghai Chemicals, China.

Preparation of Silicone Hydrogels

Bitelechelic polydimethylsiloxanes (MA-PDMS-MA) macromonomer (35 wt%), TRIS (35 wt%), DMA (30 wt%) to total 100 parts, were mixed with 20 parts of *n*-hexanol and 0.3 parts of photoinitiator Darocur 1173 and 0.5 parts of crosslinker EGDMA. The mixture was cast between two glass plates with a 0.3 mm Teflon spacer. The polymerization was carried out under UV radiation (Spectroline SB-100PC, USA) of 365 nm with a distance of 20 cm for 1 h. The polymerized membrane was soaked in ethanol to remove unreacted monomers. After immersing in fresh distilled water, transparent silicone hydrogel membrane was obtained with water content of 34 wt% measured by gravimetric assay. It has an average light transmittance of more than 95% measured by a UV-Vis Spectrophotometer (Helios, Thermo Electron Corporation) under wavelength from 400nm to 800nm. The silicone hydrogel has the tensile strength of 0.82 MPa, the Yang's modules of 2.22 MPa and the elongation at break of 69.5% measured by a Series IX Automated Materials Testing System (Instron corporation, UK) with a 10 N load cell at a cross-head speed of 10 mm/min and a constant relative humidity of 60% at 25°C.

Plasma Induced Graft Polymerization of Hydrophilic Monomers

The as-prepared silicone hydrogel membrane was wiped with a filter paper for the removal of free water on the surface and then placed in a quartz vessel of plasma treatment system (CTP-2000K Suman Electronic Company, Nanjing). The silicone hydrogel membrane was treated with atmospheric pressure glow discharge plasma (APGDP) with the power level of 60 W. Helium was used as medium of glow discharge plasma with flow rate of 5 L/min. Both surfaces of the silicone hydrogel were exposed to plasma for about 10–60 s. After plasma pretreatment, the hydrogel membrane was exposed to air for approximately 10 min to facilitate the formation of oxide and hydroperoxides^[23] on the membrane surface. The amount of hydroperoxides introduced onto the APGDP treated silicone hydrogel surface was determined according to the method as described in the literature^[11, 24]. Briefly, the hydrogel sample was immersed in isopropanol of 25 mL followed by addition of

1 mL saturated potassium iodide and 1 mL glacial acetic acid. The mixture was heated almost to boiling, kept at incipient boiling for 10 min and without cooling, titrated with standard sodium thiosulfate until the disappearance of the yellow color. It is possible to titrate a solution containing hydroperoxides as low as 10^{-4} mol/L to within 0.1 mL using 0.005 mol/L thiosulfate. Three repeats were carried out and the average amount of hydroperoxide was obtained.

NVP stock aqueous solutions of 2 wt%, 5 wt%, 10 wt%, 20 wt%, and 30 wt% were prepared and degassed with N_2 for 15 min to remove dissolved oxygen followed by addition of Mohr's salt [$FeSO_4(NH_4)_2SO_4 \cdot 6H_2O$] with concentration of 0.3 mmol/L. The APGDP treated silicone hydrogel membranes were immersed into the NVP stock solutions in a glass tube sealed with a rubber stopper. The glass tubes were then placed in a water bath of 75°C for 24 h. The membranes were washed with distilled water repeatedly to remove any unreacted monomer or physically absorbed polymer, and NVP grafted silicone hydrogel membranes abbreviated as Si-g-NVP 1 to NVP 5 were obtained as indicated in Table 1. For comparison, Si-g-0 refers to the pristine hydrophobic silicone hydrogel, and Si-APGDP is the silicone hydrogel treated with APGDP for 30 s at power of 60 W.

PEGMA grafted silicone hydrogels abbreviated as Si-g-PEGMA 1 to PEGMA 5 were also obtained by graft polymerization of PEGMA with concentrations of 2 wt%, 5 wt%, 10 wt%, 20 wt%, and 30 wt% by the same procedure as above.

Characterization of Silicone Hydrogels

The elemental composition of the surface of silicone hydrogels grafted with NVP and PEGMA dried under vacuum was analyzed using highly sensitive X-ray photoelectron spectroscopy (EscaLab 210, UK) using the monochromatized Al $K\alpha$ X-ray source (1486.6 eV photons). To compensate for surface charging effect, all binding energies (BEs) were referenced to the C 1s hydrocarbon peak at 284.6 eV.

Static water contact angles of silicone hydrogel membranes were measured by goniometer using a sessile drop method (Model JC2000C1, Shanghai Zhongchen Technology Company) after silicone hydrogels were wiped with filter paper for the removal of free water on the surface. Redistilled water was used for the measurement of static contact angles. All measurements were triplicated for each sample.

Protein adsorption of silicone hydrogels in PBS was determined by bicinchoninic acid assay (BCA Assay Kit K3000, Shanghai Biocolor BioScience & Technology Company) using bovine serum albumin (BSA)^[25]. The silicone hydrogel membrane was equilibrated in PBS for 24 h and then immersed in 3 mL of BSA solution with concentration 5.08 mg/mL in phosphate-buffered saline (pH 7.4) for 24 h at room temperature. The membrane was rinsed 3 times (10 min each) in PBS to remove loosely bound protein. The sample was then transferred into a glass tube containing 3 mL of aqueous solution of sodium dodecyl sulfate (SDS, 1 wt%) and shaken for 4 h at room temperature to release protein adsorbed on the hydrogel surface. The amount of adsorbed protein was calculated by the concentration of protein in the SDS solution proportional to the absorbance at 562 nm and a pre-set calibration curve determined by a Microplate Reader (Bio-Rad 680, USA). Three repeats were carried out and the average amount of protein adsorption was obtained.

RESULTS AND DISCUSSION

Graft Polymerization of Hydrophilic Monomers

The process for grafting hydrophilic monomer onto the surface of silicone hydrogel membranes consists of surface activation with a helium atmospheric pressure glow discharge plasma (APGDP) treatment and subsequent graft copolymerization of hydrophilic monomer. After APGDP treatment, the silicone hydrogel is exposed to air for the formation of hydroperoxides^[23]. Figure 1 shows the dependence of the concentration of hydroperoxides evolved on silicone surface on the APGDP treatment time. It is revealed that the concentration of hydroperoxides increased with increasing treatment time at the beginning of 30 s. But, the concentration increased very slowly when the plasma treatment time is over 30 s. It's assumed that hydroperoxides groups have saturated the silicone hydrogel surface after 30 s treatment. So we fixed 30 s as the APGDP treatment time for the surface activation of silicone hydrogels.

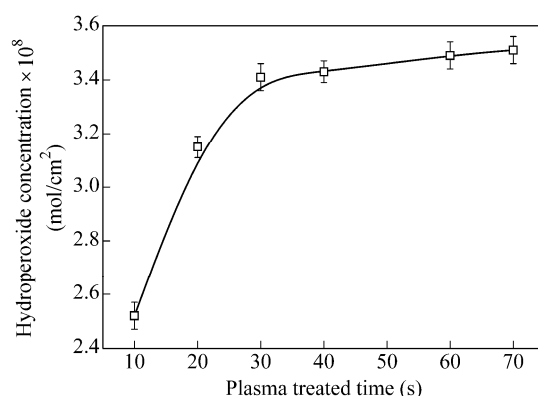


Fig. 1 Relationship between the concentration of hydroperoxides formed on silicone hydrogel surface and APGDP treatment time

The as-activated silicone hydrogels were then immersed in hydrophilic monomer solutions of *N*-vinyl pyrrolidone (NVP) and poly(oligoethylene glycol methyl ether methacrylate) (PEGMA) for graft polymerization, respectively. The polymerization conditions are summarized in Table 1. The pristine silicone hydrogel (Si-g-0) without any treatment was used as a control. APGDP treated silicone hydrogels without further surface grafting were also used for comparison. Si-g-NVP 1 to NVP 5 refer to the grafted silicone hydrogels treated in solutions with NVP concentrations of 2 wt%, 5 wt%, 10 wt%, 20 wt%, and 30 wt%. Si-g-PEGMA 1 to PEGMA 5 refer to the grafted silicone hydrogels treated in solutions with PEGMA concentrations of 2 wt%, 5 wt%, 10 wt%, 20 wt%, and 30 wt%.

Table 1. Surface graft polymerization onto silicone hydrogels after APGDP treatment for 30 s at power of 60 W and exposure to air for 10 min and protein adsorption

Samples	Concentration of hydrophilic monomer for graft polymerization (wt%)		BSA adsorption ($\mu\text{g}/\text{cm}^2$)
	NVP	PEGMA	
Si-g-0			3.09 ± 0.26
Si-g-NVP 1	2		1.60 ± 0.21
Si-g-NVP 2	5		1.09 ± 0.15
Si-g-NVP 3	10		0.81 ± 0.13
Si-g-NVP 4	20		0.80 ± 0.12
Si-g-NVP 5	30		0.79 ± 0.13
Si-g-PEGMA 1		2	1.24 ± 0.19
Si-g-PEGMA 2		5	0.88 ± 0.17
Si-g-PEGMA 3		10	0.68 ± 0.10
Si-g-PEGMA 4		20	0.52 ± 0.13
Si-g-PEGMA 5		30	0.51 ± 0.10

The surface chemical structure and composition of silicone hydrogels were analyzed by XPS spectroscopy. Figure 2 shows the surface elemental compositions of NVP grafted silicone hydrogel Si-g-NVP 3 as an example, the pristine hydrogel control (Si-g-0) and APGDP treated hydrogel (Si-APGDP) analyzed by XPS with releasing angle of the photoelectron for each atom was fixed at 20° after dehydration. Two strong peaks at 285 and 525 eV were observed for all of the silicone hydrogels, which could be attributed to C 1s and O 1s respectively. The peak at 401 eV is attributed to N 1s, and peaks at 104 and 158 eV to Si 2p and Si 2s respectively. The surface [O]/[C] ratio increased significantly after silicone hydrogel was treated with APGDP as shown in Fig. 2(b) compared with that of the pristine silicone hydrogel control of Fig. 2(a). This is due to the reaction between free radicals generated by APGDP treatment and the oxygen in air which leads to the formation of oxide and hydroperoxides on the silicone hydrogel surface. After graft polymerization of NVP onto the silicone hydrogel surface, the surface [O]/[C] ratio decreased (Fig. 2c)^[26].

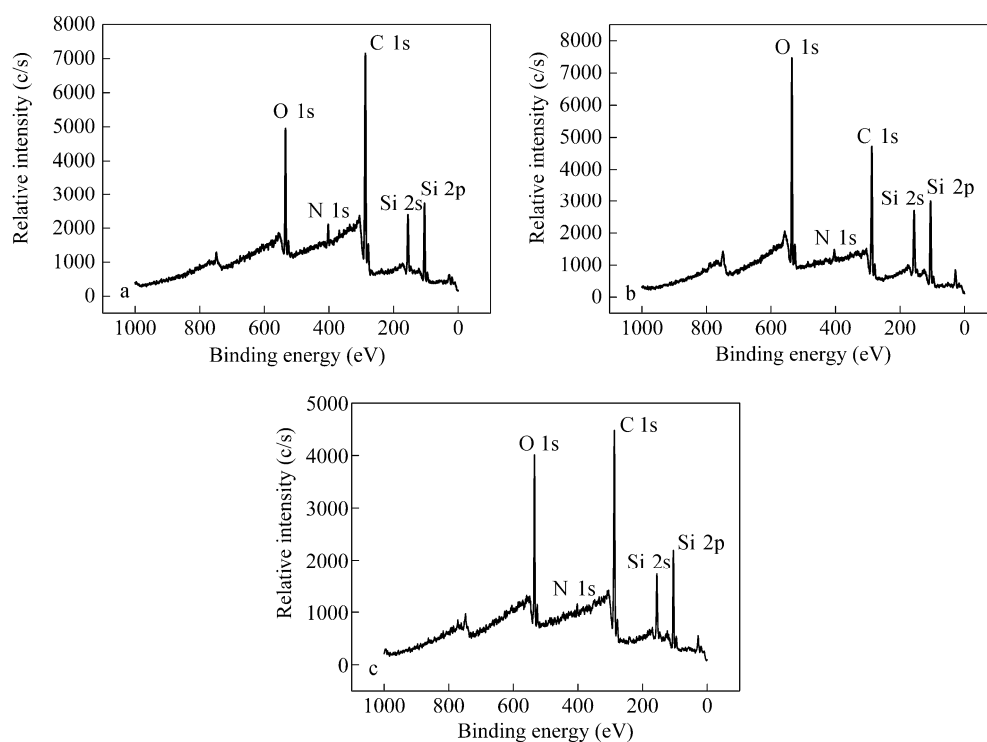


Fig. 2 Survey XPS spectra of dehydrated silicone hydrogels (a) Si-g-0, (b) Si-APGDP, (c) Si-g-NVP 3

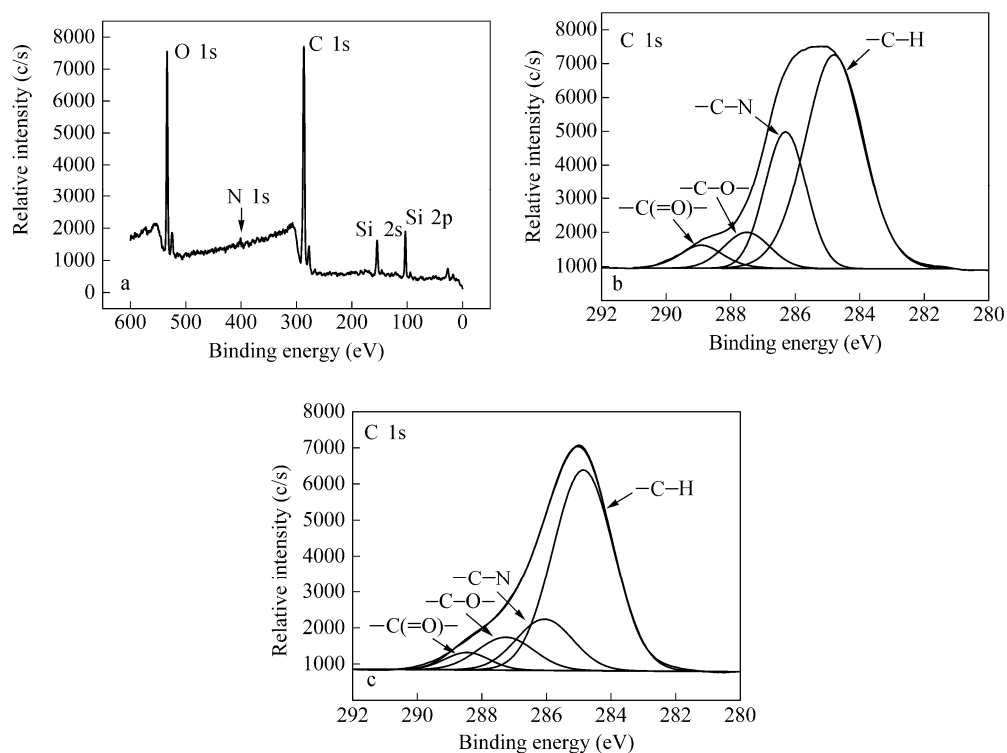


Fig. 3 Survey XPS spectra of dehydrated (a) Si-g-PEGMA 4 and high resolution C1s core-level spectra of (b) Si-g-PEGMA 4, (c) Si-g-0

Figure 3 shows the XPS spectra and high resolution C 1s core-level spectra of PEGMA grafted silicone hydrogel Si-g-PEGMA 4 as an example and the pristine hydrogel control (Si-g-0). In Fig. 3(a) of Si-g-PEGMA 4, the intensity of the peak of N 1s decreased obviously while that of O 1s increased compared with those of Fig. 2(a) of the pristine control. The high resolution C 1s core-level spectra of Si-g-PEGMA 4 (Fig. 3b) and Si-g-0 (Fig. 3c) were examined from the curve fitting spectra by a Gaussian function. The C 1s spectra included four peaks: a 284.7 eV peak corresponding to carbon with no bonds to oxygen (C—H, hydrocarbons), a 286.2 eV peak corresponding to carbon with one bond (C—N, amine), a 287.5 eV peak corresponding to carbon with one oxygen bond (C—O, ether and alcohol), and a 288.8 eV peak corresponding to carbon with three bonds to oxygen (O=C—O, ester)^[27]. Si-g-PEGMA 4 has a wider peak of C 1s spectrum (Fig. 3b). The result demonstrated the success of graft polymerization of hydrophilic monomers onto silicone hydrogel surface.

Hydrophilicity of Silicone Hydrogels

The hydrophilicity of silicone hydrogels was evaluated by the measurement of static water contact angle with a sessile drop method. Figure 4 shows the measurement of water contact angles (WCA) of surface grafted silicone hydrogels. The pristine silicone hydrogel Si-g-0 has a WCA of 103° (Fig. 4a). It means that the unmodified silicone hydrogel is hydrophobic. After graft polymerization of NVP and PEGMA, the surface of silicone hydrogel has a decrease of WCA as showed in Figs. 4(b), 4(c) and summarized in Fig. 5. The WCA of the grafted silicone hydrogel decreased with increasing concentration of hydrophilic monomers of NVP and PEGMA for the graft polymerization (Fig. 5). The NVP grafted silicone hydrogel has the WCA of about 68° with the concentration of NVP up to 10%. And the PEGMA grafted silicone hydrogels have the lowest WCA of about 62° while the concentration of PEGMA is about 20%. With further increase of hydrophilic monomer concentration, no decrease of WCA is observed (Fig. 5). The results indicate that APGDP induced grafting polymerization of NVP and PEGMA onto silicone hydrogel has optimum concentrations of 10% and 20% respectively, and the grafted silicone hydrogels are hydrophilic.

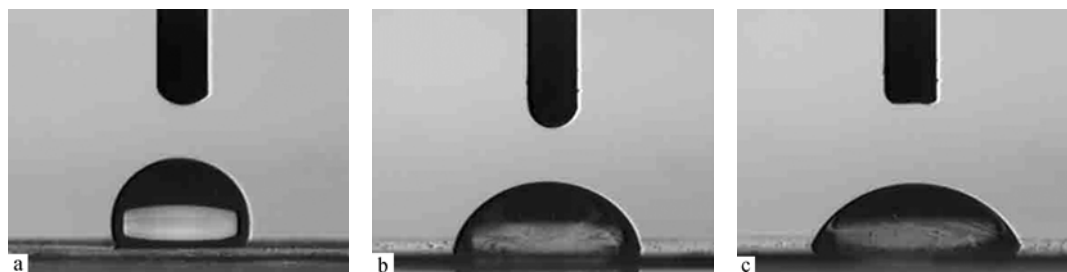


Fig. 4 Images of water contact angle measurements of (a) Si-g-0, (b) Si-g-NVP 3, (c) Si-g-PEGMA 4 as cited in Table 1

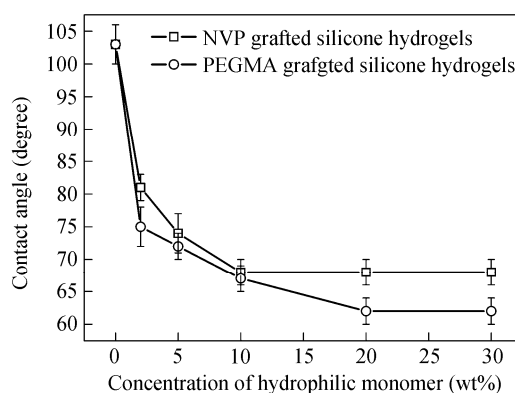


Fig. 5 Relationship between the water contact angle of silicone hydrogels prepared by APGDP induced polymerization and concentration of hydrophilic monomers of NVP and PEGMA as described in Table 1

Figure 6 shows the change of water contact angle of silicone hydrogels Si-g-NVP 3 and Si-g-PEGMA 4 as examples with time after being stored in water. We found that the silicone hydrogels grafted with hydrophilic monomers of NVP and PEGMA have no change of WCA during storage. These results indicate that the grafted silicone hydrogels have permanent hydrophilic surface. On the other hand, the silicone hydrogel (Si-APGDP) shows a WCA of 26° after APGDP treatment compared with WCA 103° of untreated control. But, the APGDP treated silicone hydrogel has a sharp increase of WCA after storage. Five days later, the WCA is approaching to that of the pristine control. So, the APGDP treated hydrogel has an approximately total recovery of surface hydrophobicity. It is assumed that the impermanent hydrophilic surface generated by APGDP treatment was owing to the formation of unstable oxygen-containing polar groups on the surface^[28].

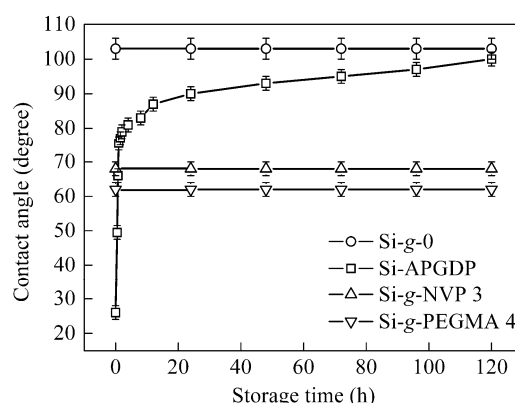


Fig. 6 Change of the water contact angle of silicone hydrogel with time after being stored in water

Protein Resistance

Protein adsorption onto the surface of the modified silicone hydrogel was measured by the method of bicinchoninic acid assay using bovine serum albumin (BSA) as a model. Table 1 shows the amount of BSA adsorbed onto the silicone hydrogel grafted with hydrophilic monomers of NVP and PEGMA. As indicated in the Table, the amount of BSA adsorbed onto the hydrophilic monomer grafted silicone hydrogel is much lower than that of the unmodified. Usually, hydrophilic surface shows relatively protein resistance^[29]. The result indicates that the grafted silicone hydrogel has the characteristics of protein resistance due to the formation of hydrophilic surface. Furthermore, the amount of BSA adsorbed onto PEGMA grafted silicone hydrogels is lower than that of NVP grafted hydrogels when hydrophilic monomer solutions with the same concentration are applied for the surface graft polymerization. It means that PEGMA grafted silicone hydrogels have superiority to NVP grafted ones for protein resistance. The results reveal that graft polymerization of hydrophilic monomers is an effective approach for the modification of silicone hydrogels in their protein resistance.

CONCLUSIONS

Surface hydrophilicity and protein resistance of silicone hydrogels were modified successfully by APGDP pretreatment followed by graft polymerization of hydrophilic monomers of NVP and PEGMA, respectively. XPS analysis confirmed the attachment of hydrophilic polymers onto the surface of silicone hydrogels. The modified silicone hydrogel has a significant enhancement of hydrophilicity with much lower water contact angle than that of the unmodified hydrogel, and the surface grafted silicone hydrogels show efficient protein resistance. APGDP induced hydrophilic monomer graft polymerization onto silicone hydrogel surface is a convenient approach to improve hydrophilicity and protein resistance for the development of silicone hydrogel soft contact lens.

REFERENCES

- 1 Bailey, C.S., *Optometry.*, 1999, 4: 26
- 2 Willcox, M.D.O. and Holden, B.A., *Biosci. Rep.*, 2001, 21: 44
- 3 Everaert, E.P., Vandermei, H.C., Devries, J. and Busscher, H.J., *J. Adhes. Sci. Technol.*, 1995, 9: 1263
- 4 Lai, J.Y., Lin, Y.Y., Denq, Y.L. and Chen, J.K., *J. Adhes. Sci. Technol.*, 1995, 10: 231
- 5 Urban, M.W. and Stewart, M.T., *J. Appl. Polym. Sci.*, 1990, 39: 265
- 6 Kuznetsov, A.Y., Bagryansky, V.A. and Petrov, A.K., *J. Appl. Polym. Sci.*, 1995, 57: 201
- 7 LÍvia, S., Diana, R. and Madalena, L., *Contact Lens & Anterior Eye*, 2007, 30: 183
- 8 Fritz, J. and Owen, M., *J. Adhes. Sci. Technol.*, 1995, 54: 33
- 9 Wavhal, D.S. and Fisher, E.R., *J. Membr. Sci.*, 2002, 209: 255
- 10 Huang, X.D., Yao, K., Zhang, H., Huang, X.J. and Xu, Z.K., *Clinical and Experimental Ophthalmology*, 2007, 35: 462
- 11 Xu, J.M., Yuan, Y.L., Shan, B., Shen, J. and Lin, S.C., *Colloids Surf. B: Biointerfaces*, 2003, 30: 215
- 12 Zhou, J., Yuan, J., Zang, X.P., Shen, J. and Lin, S.C., *Colloids Surf. B: Biointerfaces*, 2005, 41: 55
- 13 Kobayashi, T., Katou, R., Yokota, T., Suzuki, Y., Iwaki, M. and Terai, T., *Surf. Coat. Technol.*, 2007, 201: 8039
- 14 Wavhal, D.S. and Fisher, E.R., *Langmuir*, 2003, 19: 79
- 15 Sartori, S., Rechichi, A., Vozzi, G., Acunto, M.D., Heine, E., Giusti, P. and Ciardelli, G., *React. Funct. Polym.*, 2008, 68: 809
- 16 Hirotsu, T., *Thin Solid Films*, 2006, 506-507: 173
- 17 Taniguchi, M. and Belfort, G., *J. Membr. Sci.*, 2004, 231: 147
- 18 Rovira-Bru, M., Giralt, F. and Cohen, Y., *J. Colloid. Interf. Sci.*, 2001, 235: 70
- 19 Wetzels, G.M. and Koole, L.H., *Biomaterials*, 1999, 20: 1879
- 20 Wan, L.S., Xu, Z.K., Huang, X.J., Huang, X.D. and Yao, K., *Acta Biomaterialia*, 2007, 3: 183
- 21 Jones, D.S., Djokic, J. and Gorman, S.P., *Biomaterials*, 2005, 26: 2013
- 22 Lewis, A.L. and Marie, A.C., 2003, U.S. Pat., 0.152.786
- 23 Clouet, F. and Shi, M.K., *J. Appl. Polym. Sci.*, 1992, 46: 1955
- 24 Kokatmur, V.K. and Jelling, M., *J. Am. Chem. Soc.*, 1941, 63: 1432
- 25 Mequanint, K., Patel, A. and Bezuidenhout, D., *Biomacromolecules*, 2006, 7: 883
- 26 Chen, H. and Belfort, G., *J. Appl. Polym. Sci.*, 1999, 72: 1699
- 27 Hayat, U., Tinsley, A.M., Calder, R. and Clarke, J., *Biomaterials*, 1992, 13: 801
- 28 Yao, K., Huang, X.D., Huang, X.J. and Xu, Z.K., *J. Biomed. Mater. Res.*, 2006, 78: 684
- 29 Sigal, G.B., Mrksich, M. and Whitesides, G.M., *J. Am. Chem. Soc.*, 1998, 120: 3464