



Improving hydrophilicity and protein resistance of silicone hydrogel by plasma induced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine

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(Received: 22 May, 2009; published: 02 May, 2011)

Abstract: Surface properties of silicone hydrogels used as soft contact lenses play an important role in biocompatibility, conformability and deposition of protein. In this report, the surface hydrophilicity and protein deposition resistance of silicone hydrogel were modified using an atmospheric pressure glow discharge plasma (APGDP) induced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine (MPC). Silicone hydrogel was treated with plasma and exposed to air to form oxide and hydroperoxides at the surface, which initiated surface graft polymerization of MPC. Elemental composition and structure at the surface of silicone hydrogel were characterized through ATR-FTIR and XPS. The data of ATR-FTIR and XPS analyses revealed that MPC was grafted onto the surface of silicone hydrogel. Contact angle measurement was used to evaluate the hydrophilic property of the silicone hydrogel. The MPC grafted silicone hydrogel has the contact angle about 55° when MPC solution with the concentration 10 wt% is applied for graft polymerization. The result showed that graft polymerization of MPC improved the hydrophilicity of silicone hydrogel efficiently. Bovine serum albumin (BSA) was used as a model to investigate protein deposition resistance of the modified silicone hydrogel. The data obtained by bicinchoninic acid assay revealed that the grafted silicone hydrogels had a significant enhancement of protein resistance.

Keywords: silicone hydrogel, graft polymerization, plasma, hydrophilicity, protein resistance

Introduction

Silicone hydrogels have attracted much attention as new generation of soft contact lens in the past decade [1]. They may provide sufficient supply of oxygen to the cornea for the metabolic requirements. However, the surface of silicone hydrogel is hydrophobic and this results in poor compatibility with the ocular environment. There is a need to design the surface structure and properties of silicone hydrogels to be compatible with the corneal epithelium environment to enhance conformability and anti-deposition of protein. One strategy is surface modification that should improve hydrophilicity and protein deposition resistance of silicone hydrogels.

Plasma treatment, particularly low-pressure plasma, is one of the most versatile techniques in surface modification of polymers. Low-pressure plasma treatment creates polar groups (–COOH, –OH), increases the surface energy and wettability, and also enhance implant biocompatibility [2]. It has been used to improve the silicone polymers hydrophilicity without changing their bulk material properties [3-5].

Owen M J et al [6] reported N₂ and oxygen plasma treatment of silicone rubber surfaces. Williams R L [7] further studied the structural stability of Ar plasma-treated silicone rubber surface and its influence on the interfacial aspects of blood compatibility. But, plasma treatments are often used at dry state and give unstable hydrophilic surface. Fritz J et al [8] shown hydrophobic recovery of plasma treated PDMS surface with various gases like oxygen, argon, nitrogen and helium as medium. It is reported that low pressure plasma treatment has also been applied to silicone hydrogel contact lenses commercially available [9]. Atmospheric pressure glow discharge plasma (APGDP) maintains the positive aspects of vacuum plasma treatment. Compared with low pressure plasma treatment, APGDP applied thorough a torch is a highly versatile industrial alternative to be integrated in an existing production line [10]. This treatment is useful to activate the surface and even initiate graft polymerization of hydrophilic monomers to enhance surface hydrophilicity.

Grafting of hydrophilic moieties onto polymer surface is an efficient approach to improve hydrophilicity and biocompatibility. Hydrophilic moieties can be attached to the surface of polymers by graft polymerization of hydrophilic monomers after initiating with ozone, ion sputter and plasma. 2-Methacryloyloxyethyl phosphorylcholine (MPC) is regarded as a biomimetic component of cell membrane [11]. The excellent hydrophilicity and biocompatibility of MPC containing polymers has been confirmed by various phenomena such as being quite inert in biological systems, reducing protein absorption, inhibiting bacterial adhesion, and suppressing cell attachment [12-14]. Polymers modified with MPC have great potential for a wide range of medical applications because of the enhancement of hydrophilicity [15-17]. Goda et al [18] investigated photo-induced grafting of MPC onto silicone rubber. Jianmin Xu et al [19] used ozonization technology to active the surface of silicone rubber and then induced MPC grafted polymerization to obtain a blood compatible surface. However, to our knowledge, there are until now no reports of plasma induced graft of MPC onto silicone hydrogel for the development of soft contact lens with enhanced hydrophilicity and protein resistance.

In this work, surface modification of silicone hydrogels by APGDP induced MPC grafting was investigated in order to improve hydrophilicity and anti-deposition of protein for the development of soft contact lenses. The surface structural change of plasma induced MPC graft polymerization of silicone hydrogel was characterized by ATR-FTIR and XPS. And the hydrophilicity and protein resistance of MPC grafted silicone hydrogel were evaluated by water contact angle and bovine serum albumin (BSA) adsorption assay.

Results and discussion

APGDP induced graft polymerization of MPC

Plasma induced graft polymerization of monomers is a versatile technique for the surface modification of polymer materials. The process of APGDP treatment and graft polymerization of MPC onto silicone hydrogel surface is schematically shown in Figure 1. Helium was used as medium to obtain stable atmospheric plasma. Silicone hydrogel with the water content of 34 wt.% was treated with APGDP and then exposed to air for the formation of hydroperoxides [21]. The surface of hydrogel was further modified by graft polymerization of MPC initiated with hydroperoxides. The change in chemical structure and composition on the silicone hydrogel surface was characterized by XPS and ATR-FTIR spectroscopy in detail as follows.

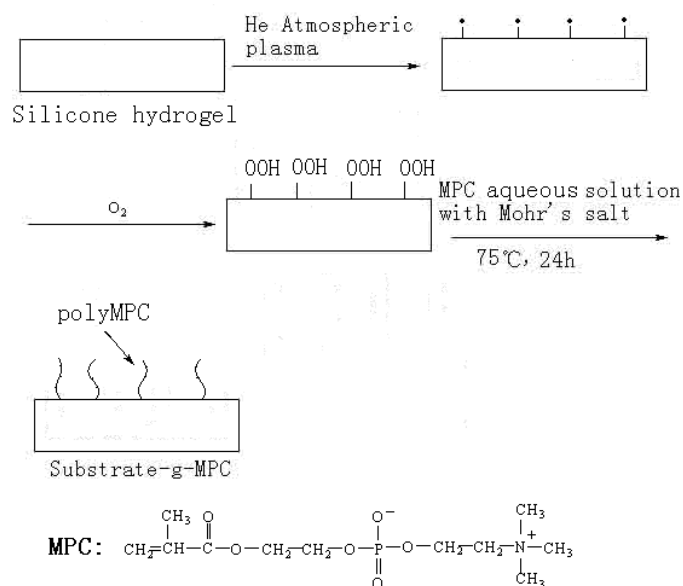


Fig. 1. Schematic presentation of atmosphere plasma induced graft polymerization of MPC onto silicone hydrogel surface.

XPS analysis

Figure 2 shows the XPS spectra of silicone hydrogels at dry state. Pristine silicone hydrogel has two strong peaks centered at 285 and 525 eV (Figure 2(a)), which can be attributed to C 1s and O 1s respectively. The peaks at 104 and 158 eV due to Si 2p and Si 2s respectively were also obvious, and the peak at around 400 eV is attributed to N 1s.

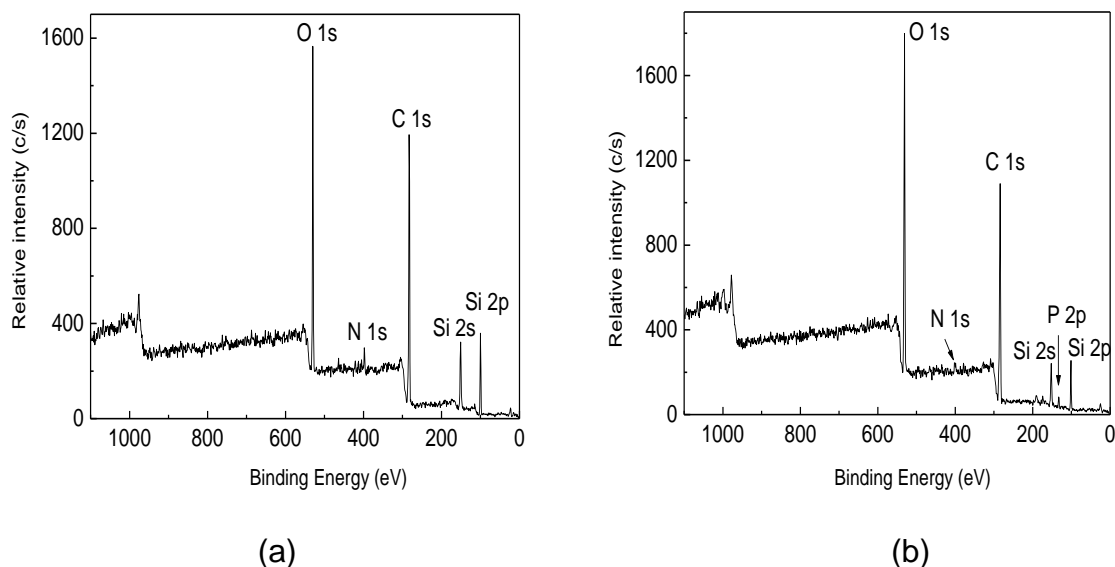


Fig. 2. Survey XPS spectra of dehydrated (a) pristine silicone hydrogel, and (b) MPC-grafted silicone hydrogel prepared by plasma pretreatment with power 60W for 30 s and then surface graft polymerization with MPC with concentration 10 wt.% at 75 °C for 24 h.

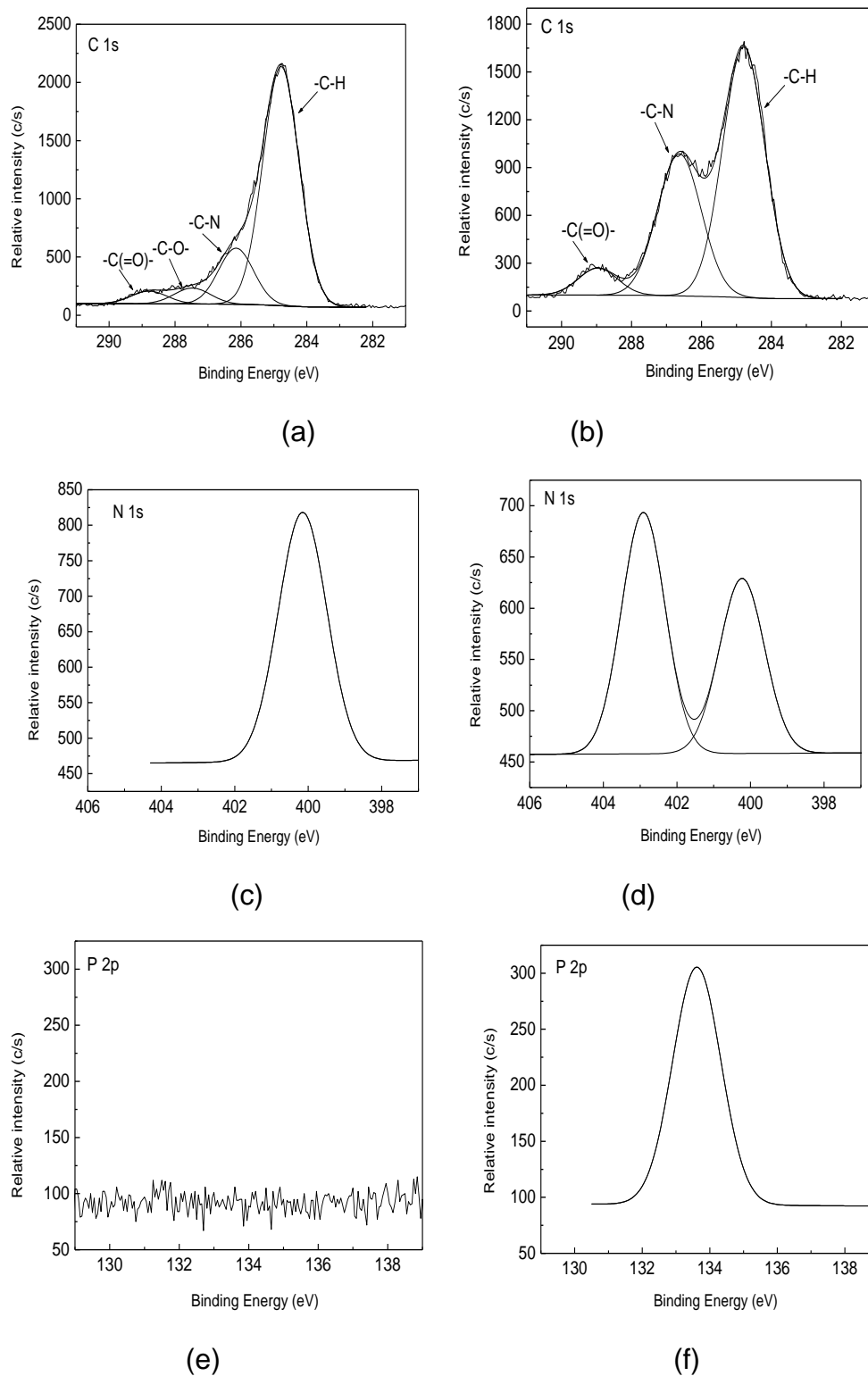


Fig. 3. Elemental core-level spectra of (a), (c), (e): pristine silicone hydrogel and (b), (d), (f): MPC-grafted silicone hydrogel prepared by plasma treatment with power 60 W for 30 s and then surface graft polymerization of MPC with concentration of 10 wt.% at 75 °C for 24 h.

The MPC-grafted silicone hydrogel prepared by plasma treatment and following surface graft polymerization of MPC has a new peak centred at 137 eV (Figure 2(b)), which can be ascribed to P 2p of the phospholipid moiety of the MPC polymer grafted onto the surface of silicone hydrogel [23]. The elemental composition of silicone hydrogel surface can be summarized as shown in Table 1. The content of P 2p at the grafted silicone hydrogel surface is as high as 2.31%. This result confirmed the success of plasma induced graft polymerization of MPC at the silicone hydrogel surface.

Tab. 1. Surface elemental composition of silicone hydrogel at dry state determined by XPS.

Sample*	C (%)	O (%)	Si (%)	N (%)	P (%)
pristine silicone hydrogel	51.26	24.49	16.41	7.84	0
MPC-grafted silicone hydrogel**	51.05	21.32	15.15	10.17	2.31

* Sample is dehydrated before XPS analysis

** MPC-grafted silicone hydrogel was obtained by plasma treatment with power 60W for 30s and then surface graft polymerization of MPC with the concentration of 10 wt.% at 75 °C for 24 h.

The percentages of various functional groups of MPC grafted onto the silicone hydrogels were evaluated from the curve fitting spectrum by a Gaussian function with peak position and FWHM kept constant. The high resolution C 1s, N 1s and P 2p core-level spectra were examined. Representative C 1s spectrum for the pristine silicone hydrogel surface is shown in Figure 3(a). The C 1s peak was deconvoluted into four peaks: a 285.0 eV peak corresponding to carbon with no bond to oxygen (C–H, hydrocarbons), a 286.4 eV peak corresponding to carbon with one bond (C–N, amine), a 287.7 eV peak corresponding to carbon with one oxygen bond (C–O, ether and alcohol), and a 289 eV peak corresponding to carbon with three bonds to oxygen (O=C–O, ester) [24]. After graft polymerization of MPC onto the surface of silicone hydrogel, we did not observe the peak of 287.7 eV corresponding to carbon with one oxygen bond (C–O, ether and alcohol) in the C 1s spectrum as shown in Figure 3(b). But, the intensity of peaks at 286.4 eV and 289 eV increased significantly (Figure 3(b)). In the N 1s core-level spectrum of pristine silicone hydrogel, an intense peak of 400.2eV is observed corresponding to amide (N–C=O) (Figure 4(c)). While an additional peak at 402.9 eV is shown in the N 1s core-level spectrum of the modified silicone hydrogel (Figure 4(d)), which can be attributed to the N⁺(CH₃)₃ groups of grafted MPC moieties [25]. Besides, in the P 2p core-level spectrum an intense peak at 133.6 eV is observed attributable to (PO₄⁻) (Figure 4(f)). These results indicate that phospholipid moieties have been introduced onto the silicone hydrogel surface by the plasma induced graft polymerization of MPC.

ATR-FTIR spectra analysis

Figure 4 shows the ATR-FTIR spectra of silicone hydrogels at dry state. The pristine silicone hydrogel surface has a peak centered at 1259 cm⁻¹ (Figure 4(a)) that can be attributed to –Si–CH₃ vibration, and a peak at 1015 cm⁻¹ due to –Si–O–Si– absorption. In addition, the peaks at 1650 cm⁻¹ and 1725 cm⁻¹ can be ascribed to –CON(CH₃)₂ and –COO– absorption respectively. After MPC was grafted onto the surface, the ATR-FTIR spectrum shows characteristic absorption of graft polymer of

MPC as shown in Figure 4(b-d). The peak at 1240 cm^{-1} can be attributed to $-\text{POCH}_2$ group vibration. And, $-\text{N}^+(\text{CH}_3)_3$ and $-\text{COO}-$ absorption peaks were observed at 970 cm^{-1} and 1725 cm^{-1} , respectively. Besides, the broad peak at 3400 cm^{-1} related to the $-\text{OH}$ absorption become stronger after MPC grafting [26]. The data further confirmed graft polymerization of MPC onto the silicone hydrogel surface.

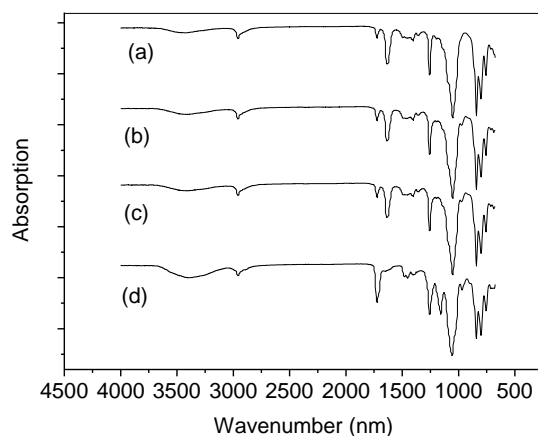


Fig. 4. ATR-FTIR spectra of dehydrated (a) pristine silicone hydrogel, and MPC-grafted silicone hydrogel with MPC concentration (b): 1 wt.%; (c): 5 wt.%; (d): 10 wt.%, respectively. Preparation of MPC-grafted silicone hydrogel: plasma retreatment with power 60 W for 30 s and then surface graft polymerization at $75\text{ }^\circ\text{C}$ for 24 h.

Hydrophilicity of silicone hydrogel

Water contact angle is a convenient parameter to characterize the hydrophilic/hydrophobic property of silicone hydrogel. Figure 5 shows the change of water contact angle of silicone hydrogels before and after treatment. Although pristine silicone hydrogel is prepared by copolymerization of silicone monomer and hydrophilic monomer DMA with weight ratio of 30%, we found that it has a WCA of 103° . The result reveals that pristine silicone hydrogel is hydrophobic. After APGDP treatment without following MPC grafting, the treated silicone hydrogel has a WCA decreased to 26° . It can be ascribed to the formation of hydrophilic groups such as hydroperoxides at the surface after plasma treatment [27]. But, a significant recovery of WCA is observed after plasma treated hydrogel stored for several days. Especially, the treated hydrogel has a total recovery of hydrophobicity after 15 days. This may indicate the instability of hydrophilic groups such as hydroperoxides formed at the surface of silicone hydrogel during plasma treatment. So, APGDP treatment cannot permanently enhance hydrophilic property of silicone hydrogel.

When silicone hydrogel was treated by a combination of APGDP and following graft polymerization of MPC at the surface, it shows a decrease of WCA as compared with pristine silicone hydrogel as indicated in Figure 5. While MPC solution with the concentration of 1 wt.% is used for the graft polymerization, the silicone hydrogel has a WCA about 80° . As the concentration of MPC increases, the WCA of silicone hydrogel decreases apparently. When MPC concentration is 10 wt.%, the treated silicone hydrogel has a WCA of about 55° , which shows excellent hydrophilicity. We also found that only a very small increase of WCA is observed after treated hydrogel

is stored for 15 days. It means graft polymerization of MPC at the surface maintains the hydrophilicity of silicone hydrogel efficiently. This may be attributed to crosslinking attachment of MPC to the silicone hydrogel surface through grafted polymerization [23].

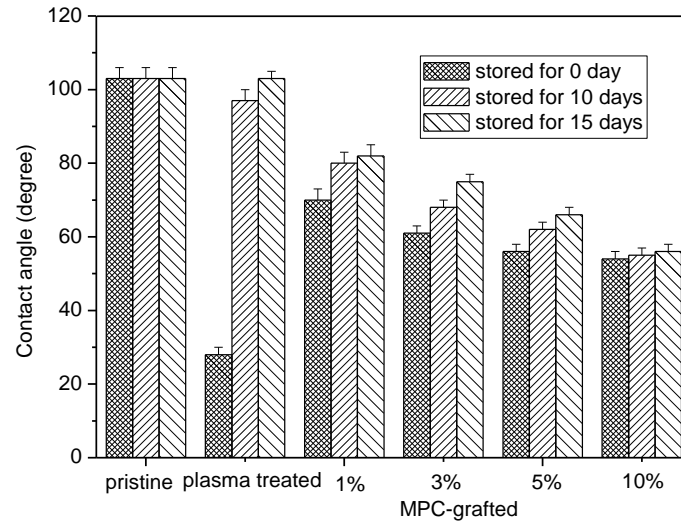


Fig. 5. Change of water contact angle of pristine, plasma treated and MPC-grafted silicone hydrogel after stored for 0, 10, 15 days. “Plasma treated” silicone hydrogel was obtained by plasma treatment with power of 60W for 30s. “1%, 3%, 5%, 10% MPC-grafted” silicone hydrogel was obtained by APGDP treat with power 60W for 30s and then surface graft polymerization of MPC with the concentration of 1%, 3%, 5% ,10% at 75 °C for 24 h.

The crosslinked MPC cannot be buried in the top surface through chain rotation. As a comparison, silicone hydrogel with no experience of plasma pretreatment are subjected to the graft polymerization procedure with MPC concentration of 10 wt.%. We found that it has a WCA of 103° the same as that of the pristine silicone hydrogel. It is concluded that the surface of silicone hydrogel could not be activated without plasma treatment. Therefore, a combination of APGDP and MPC graft polymerization can permanently improve hydrophilic property of silicone hydrogel.

Bulk properties of silicone hydrogel

Optical and mechanical properties are other important factors that are required for materials for contact lenses. The present work focus on the surface modification of silicone hydrogels by APGDP induced MPC grafting. Figure 6 shows the optical tendencies of silicone hydrogels before and after treatment. All silicone hydrogels have transmittance of more than 92% with the wavelength range from 400 nm to 800 nm. The results indicate that the as-prepared silicone hydrogels are transparent although the surface of the silicone hydrogel is modified. It is concluded that the excellent optical transparency of the silicone hydrogel could be kept regardless of surface modification through APGDP induced MPC graft polymerization.

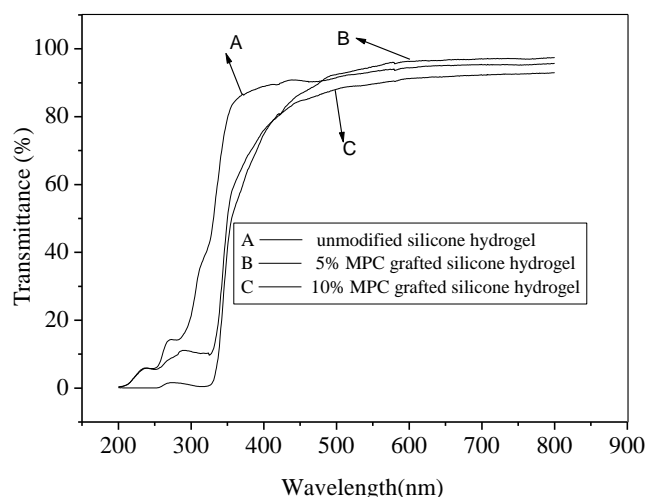


Fig. 6. Optical properties of silicone hydrogels.

Table 2 shows the mechanical properties of silicone hydrogels. It can be seen that the pristine silicone hydrogel had tensile strength of 0.82 MPa, Yang's modulus of 2.02 MPa. After plasma induced graft polymerization of MPC onto the surface, the silicone hydrogels show almost no difference of tensile strength and Yang's modulus compared with the pristine sample. These results indicated that the atmospheric pressure glow discharge plasma induced graft polymerization method described in this work would not destroy the bulk mechanical property of the silicone hydrogel.

Tab. 2. Mechanical properties and BSA adsorption of silicone hydrogels.

Silicone hydrogel	Tensile strength (MPa)	Yang's modulus (MPa)	BSA adsorption ($\mu\text{g}/\text{cm}^2$)
Pristine	0.82 ± 0.09	2.02 ± 0.04	3.09 ± 0.26
MPC grafted 1*	0.83 ± 0.07	2.03 ± 0.04	0.88 ± 0.16
MPC grafted 2*	0.84 ± 0.05	1.93 ± 0.06	0.66 ± 0.06
MPC grafted 3*	0.83 ± 0.09	1.85 ± 0.05	0.55 ± 0.11

* MPC grafted 1, 2, 3: silicone hydrogels obtained by plasma treatment at power 60W for 30s and then surface graft polymerization of MPC with the concentration of 1 wt.%, 5 wt.% and 10 wt.% at 75 °C for 24 h respectively.

Protein resistance

Table 2 shows the adsorption of BSA onto silicone hydrogel surface. As indicated in the table, protein adsorbed at the MPC grafted silicone hydrogel is much lower than that of the pristine silicone hydrogel. When silicone hydrogel was treated by APGDP followed by graft polymerization of MPC with the concentration of 10 %, it has the lowest BSA adsorption of $0.55 \pm 0.11 \mu\text{g}/\text{cm}^2$. So, MPC grafted silicone hydrogel shows protein resistance. It is attributed to the hydrophilic surface of the modified silicone hydrogel [28]. The result demonstrates that graft polymerization of MPC onto silicone hydrogel surface is an effective approach for the development of silicone hydrogel with improved protein resistance.

Conclusions

The surface of silicone hydrogel was modified successfully by atmospheric pressure glow discharge plasma (APGDP) pretreatment followed by MPC graft polymerization. ATR-FTIR and XPS analysis confirmed the attachment of MPC moiety onto the silicone hydrogel surface. Contact angle measurement proved that the modified silicone hydrogel could be permanently hydrophilized. The surface modified silicone hydrogel by graft polymerization of MPC shows an efficient protein deposition resistance. Therefore, plasma induced MPC graft polymerization onto the silicone hydrogel surface is a promising convenient approach to improve hydrophilicity, protein deposit resistance for the development of silicone soft contact lens.

Experimental part

Materials

Bitelechelic polydimethylsiloxanes (MA-PDMS-MA) macromonomer was synthesized by ring opening reaction of glycidyl methacrylate (GMA, Shanghai Heshibi Chemicals, china) with amine ended polydimethylsiloxanes [20](KF8010, Shin-Etsu Chemicals, Japan). 3-Methacryloxypropyl tris(trimethylsiloxy silane) (TRIS) (98%) was purchased from Alfa Aesar. N,N-Dimethyl acrylamide (DMA) and ethylene glycol dimethacrylate (EGDMA) was purchased from Shanghai Heshibi Chemicals, China. 2-Methacryloyloxyethyl phosphorylcholine (MPC) was supplied from Nanjing Letian S&T Development Company. Photoinitiator Darocur 1173 was CIBA product. Ammonium peroxodisulfate was supplied from Shanghai Chemical Regents, China.

Preparation of silicone hydrogel

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 sealed with a 0.3-mm Teflon spacer. The polymerization was carried out under an UV radiation (Spectroline SB-100PC, USA) of 365 nm with a distance of 20 cm from lamp to sample for 1 hour. Then, the polymerized membrane was soaked in ethanol to remove unreacted monomers. After immersing in fresh distilled water, transparent silicone hydrogel membrane was obtained. The water content of silicone hydrogel is 34 wt.% measured by gravimetric assay.

Plasma treatment and graft polymerization of MPC

The as-prepared silicone hydrogel membrane was wiped with a filter paper to remove free water at the surface and then placed in a quartz vessel of APGDP treatment system (CTP-2000K Suman Electronic Company, Nanjing). The plasma system was equipped with two parallel electrode plates and the quartz vessel was sandwiched by the electrode plates. Helium was used as medium of glow discharge plasma and flow through the quartz vessel with the rate of 5 L/min at atmospheric pressure. Both surfaces of the silicone hydrogel membrane was treated with atmospheric pressure glow discharge plasma for about 30 s with power level 60 W. After plasma treatment, the hydrogel membrane was exposed to air for approximately 10 min to facilitate the formation of oxide and hydroperoxides [21] at the surface. The APGDP treated silicone hydrogel was used for further grafting.

MPC stock aqueous solutions of 1, 3, 5, and 10% (wt%) were prepared and degassed with N₂ for 15 min to remove dissolved oxygen followed by addition of Mohr's salt [FeSO₄(NH₄)₂SO₄·6H₂O] with concentration of 0.3 mM. The APGDP treated silicone hydrogel membrane was immersed into the MPC stock solution in a glass tube sealed with a rubber stopper. For comparison, pristine silicone hydrogel membrane without plasma treatment was used as control which experienced the same procedure as the APGDP treated silicone hydrogel. The glass tube was then placed in a water bath of 75 °C for 24 h. The silicone membrane was then washed with distilled water thoroughly to remove unreacted monomer and physically absorbed polyMPC, and MPC-grafted silicone hydrogel was obtained.

Characterization of silicone hydrogel

The surface elemental composition of the silicone hydrogel after dehydration in an oven at 105 °C for 24 h was analyzed using X-ray photoelectron spectroscopy (EscaLab 210, UK) using the monochromatized Al K α 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. Elemental core-level spectra were curve-fitted by a Gaussian function. Surface IR spectrum of silicone hydrogel at dry state was measured with ATR- FTIR spectrophotometer (Nicolet, USA).

Water contact angles were measured at room temperature using a sessile drop method (Model JC2000C1, Shanghai Zhongchen Technology Company) after silicone hydrogels were wiped with filter paper to remove free water at the surface. All measurements were triplicated for each sample. Redistilled water was used for the measurement of static contact angle.

The optical transparencies of the hydrogels swelled in distilled water were measured using a Vis/UV spectrophotometer (Helios UV Visible Spectrophotometers, Thermo Electro Corporation, USA) in the wavelength range of 200–800 nm. Samples completely swelled by distilled water were placed in a quartz cell and transparencies were measured at 25 °C.

Tensile tests of silicone hydrogels were performed using a Series Automated Materials Testing system (Instron corporation, UK) with a 10N load cell in a constant relative humidity (60%) room at 25 °C. The thickness of these samples was measured with a digital micrometer having a precision of 1 μ m. A cross-head speed of 10 mm/min was used and at least three samples were tested for each silicone hydrogel.

Protein adsorption

Protein adsorption at the surface of silicone hydrogel was determined by bicinchoninic acid assay (BCA Assay Kit K3000, Shanghai Biocolor BioScience & Technology Company) using bovine serum albumin (BSA) [22]. The silicone hydrogel membrane was equilibrated in PBS for a period of 24 h and then immersed in 3 ml BSA solution with concentration 5.08 mg/ml in phosphate-buffered saline (pH 7.4) for 24h at room temperature. The membrane was rinsed 3 times (10 min each) in PBS to remove loosely bound BSA. The sample was then transferred into a glass tube containing 3 mL of 1-wt % aqueous solution of sodium dodecyl sulfate (SDS) and shaken for 4 h at room temperature to release BSA adsorbed on the hydrogel surface. The amount of adsorbed BSA was calculated from the concentration of BSA

in the SDS solution read at 562 nm and a calibration curve prepared from a pure sample measured by a Microplate Reader (Bio-Rad 680, USA). Three repeats were measured and the average value of adsorbed protein was taken.

Acknowledgements

The authors are grateful for Hydron Contact Lens Co., Ltd and National Natural Science Foundation of China for financial support of project 50673019.

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