Analysis and Evaluation of the Ionic Interaction of the Novel Soft Contact Lenses Using the Zwitterionic Polymer Gel

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ABSTRACT: In the zwitterionic polymer gel which has cationic and anionic groups inside, it forms a complex to producing stability by adding thermal energy. We reported the behavior induced by the ionic interaction of them and the impact that a nonionic surfactant could exert on the complex formation. We had heating experiments of the zwitterionic polymer gel in PBS with a nonionic surfactant added. We analyzed DSC and measured the diameter, stress and flexure of heated the gel. As the result, it has been demonstrated that formation of strong ionic interactions inside the gel can be achieved by heating them in a solution containing the nonionic surfactant. It has been also demonstrated that the ratio of bound water is increased within the gel, promising an enhanced strength. © 2009 Wiley Periodicals, Inc. J Appl Polym Sci 114: 2764–2768, 2009

Key words: biomaterials; hydrogels; surfactants; hydrophilic polymers

INTRODUCTION

Polymer gels have been investigated for practical applications as soft and wet material. One feature of a polymer gel is its water absorbance property. Commercialization has been sought since long time ago based on this water absorbance characteristic of a polymer gel. Major examples of such commercialization include soft contact lenses (SCL), toiletry products with high-absorbent resin, cosmetics, inks, fragrances.[1–3] Among them, SCL has been developed from the standpoint of biomimicry. With the cornea assumed as one form of hydrous gel constitutes of proteins or others, SCL mimics corneal structure and features to enhance its affinity with the cornea for improved safety and comfort.

SCL is a hydrous gel, has therefore high bioaffinity, and has been commercialized as a polymer material to directly contact membranes.[4] Old SCL materials used to employ 2-hydroxyethly methacrylate (HEMA) as their constituent, then ionic polymer gels emerged, produced by copolymerization of methacrylic acid (MAA) and HEMA aiming at approximate the water content of the human cornea. However, the inclusion of MAA rendered materials negatively charged and caused their ionic interaction with cationic proteins in the tear film represented by lysozyme. The interaction resulted in deposition of the proteins on the lens surface and has led to reports on adverse events such as infection or blurred vision. To obtain a high water-content polymer gel while addressing these problems, applicability to a contact lens of a zwitterionic polymer gel with an equimolar content of cationic and anionic monomers in the high weight molecule has been reported.[5] The zwitterionic polymer gel is unique among high water-content SCL. It has both cationic and anionic functional groups. Its higher resistance to soilants and superior stability against environmental changes compared with the traditional anionic SCL have been reported.

In a recent report on the other hand, the zwitterionic SCL was utilized in a drug delivery system (DDS).[6–9] In the report, the drug is encapsulated in the hydrous gel through the ionic interaction between the cationic functional groups in SCL and the anionic drug substance. Repeated exchange reactions between tear film ions and the drug initiate gradual release of the drug into the eye. The anionic functional groups on the other hand, restrain the reaction of the electric charge inside the hydrous gel and render the lens dimensional stability and durability.

This zwitterionic polymer gel has, when hydrated, its cationic group and anionic group inside separate from each other at a certain distance. This separation makes the size of lens larger and the density lower. With the addition of thermal energy on the other hand, counterions attract each other to produce

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stability. In this state, the lens contracts and becomes denser. In other words, the lens has a characteristic that it forms a complex by reducing interionic distances.

In this study, therefore, considering the behavior induced by the ionic interaction that the zwitterionic polymer gel exhibits, we will report the impact that a nonionic polymer surfactant could exert as a possible external factor on the complex formation among the ions contained in the polymer gel.

EXPERIMENTAL

Materials

2-Hydroxyethyl methacrylate (HEMA) was obtained from Mitsubishi gas Chemical Company, Inc. (Tokyo, Japan), 2-hydroxypropyl methacrylate (HPMA) and ethyleneglycol dimethacrylate (EDMA) from Mitsubishi Rayon Co., Ltd. (Tokyo, Japan). For the cationic monomer, methacrylamidopropyltrimethylammonium chloride(MAPTAC) from Mitsubishi Rayon Co., Ltd., was used and methacryloyl oxyethyl hydrogen succinate (MOESA) from Kyoeisha Chemical Co., Ltd. (Osaka, Japan), for the anionic monomer. 2,2′-Azobisisobutyronitrile (AIBN) from Wako Pure Chemical Co., Ltd. (Osaka, Japan) was used for the polymerization initiator, and polyoxy/polyoxyethylene (196) polyoxypropylene (67)glycol from BASF Ltd. (USA), as the nonionic surfactant. These structures are shown in Figure 1.

Sample synthesis

According to the previous reports,[6,10] HEMA 50.0%, HPMA26.5%, MAPTAC 12.2%, MOESA 10.3%, EDMA 1.0%, and AIBN 3500 ppm were mixed and stirred for 1 h under a nitrogen. The liquid monomer mixture was poured into the CL mold, heated in the range of 50–100°C for 24 h to obtain a polymer. The polymer was cooled to room temperature, removed from the container, and then soaked in distilled water at ~ 60°C for about 4 h for hydration. According to the previous reports,[5,11] the water content of SCL, the Dk (oxygen permeability), the refractive index was measured (Table I).

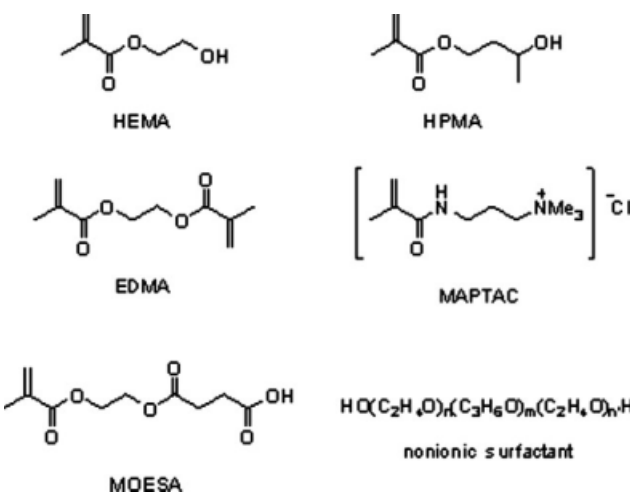

Figure 1 The structure of materials.

TABLE I
Quality of SCL

Water content	56(%)
Refractive index	1.406
Luminous transmittance	98%
Oxygen permeability	30×10^{-11} (cm^2 sec^{-1}) × ($mL(O_2)/mL \times mmHg$)

Heating experiment of zwitterionic SCL

Zwitterionic SCL hydrated in the phosphate buffer solution (PBS) with a nonionic polymer surfactant added was heated at 121°C. The quantities of the nonionic surfactant added were 0% (blank), 0.005%, 0.01%, while the heating time were 1, 5, 10, and 30 minutes. The FTIR using KBr method and the contact angle of each samples was measured.

Measurement of SCL dimension, stress, and flexure

In the course of the above-mentioned heating tests, the diameter of heated SCL was measured with a Dimension analyzer (Optimec Ltd.) in PBS (pH 7.0) at 20°C.

Stress and flexure were measured with the Tabletop Precision Tester AG-5A (Shimazu Co., Ltd.)[9] SCL was processed into 2.0 mm wide and 0.5 mm thick strips and measured at a velocity of 100 mm/min.

Observation of the state of water within polymer gel

SCL of 5 mg was weighed, sealed in an aluminum airtight container, and then subjected to thermal analysis by Differential Scanning Calorimetry (DSC). Measurement conditions were from −50 to 100°C for the temperature range and 5°C/min for the rate of temperature rise. As Figure 2 indicates, peaks were classified into the free water peak with a melting point in the vicinity of 0°C and the bound water peak with a melting point lower than 0°C. The ratio of the presence of two types of water was calculated based on the ratio of the melting peak areas.

RESULTS AND DISCUSSION

The zwitterionic polymer gel is known to contract by forming a complex, initiated by the addition of energy in the form of heat or others, which strengthens interionic interaction. The process is outlined

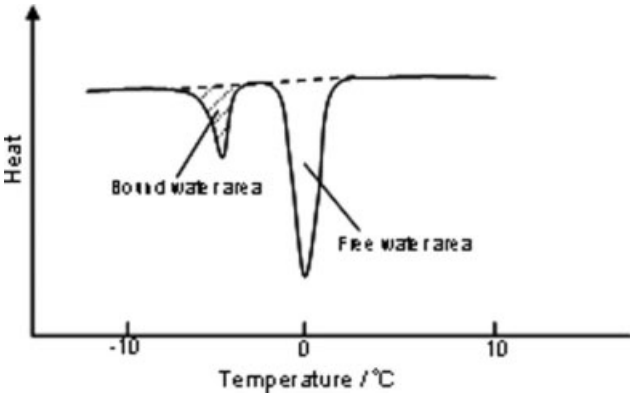

Figure 2 Modulated temperature DSC thermograms of SCL. The abundance ratio of bound water and free water were calculated from respective areas.

in a drawing as Figure 3. The shape of the gel is stabilized by thus formed complex. To control the formation of this complex, first the nonionic surfactant was added to the staffing solution during the thermal treatment of the zwitterionic polymer gel, and the relationship between heating time and lens diameter was determined at each concentration. Results are shown in Figure 4. First strong interaction between anionic and cationic groups was induced by the heat treatment, then shrinkage of the distance between the two groups followed, making SCL shrink. Then, in the 1 minute heating, rate of lens shrinkage declined with increased concentrations of the nonionic surfactant. This indicates that, in an earlier stage of heating, the interionic interaction inside the hydrous gel was hampered by the nonionic surfactant which has high latitude, failing to develop, therefore, strong enough to contract the interionic distance. On the other hand, with the 5 minutes or longer sterilization, the rate of lens constriction was similar among concentrations. It is indicated that sufficient energy for the development of interionic interaction supplied by the prolonged sterilization and complex was formed under the presence of a nonionic surfactant. Figure 5 shows the relationship of the amount of nonionic surfactant added and the gel size at 1 and 30 minutes of heating. The results also indicate that around 30 minutes of heating can form a complex independent of the

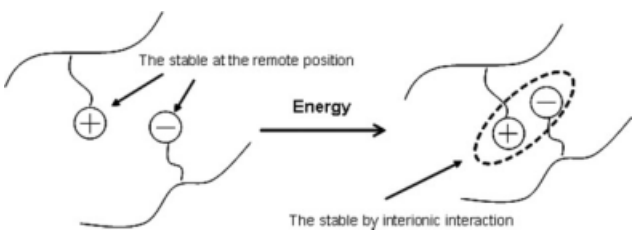

Figure 3 The outline of changing shape of the zwitterionic polymer gel during the thermal treatment.

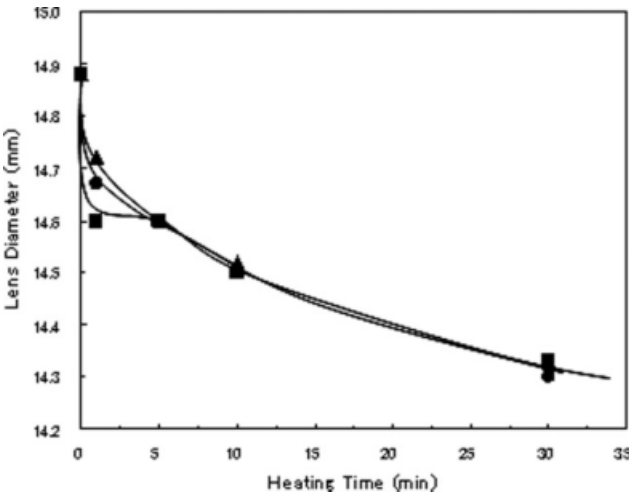

Figure 4 The relationship between heating time and lens diameter. The quantities of nonionic surfactant added were 0, 0.005, 0.01%.

amount of nonionic surfactant added. Results have shown that the formation of complex among counterions present on the hydrous gel varies depending on the environment.

Results in Figure 4 and 5 indicate that 30 minutes heating allows the formation of a stable complex independent of the concentration of the nonionic surfactant. To understand the state of water within the hydrous gel in the process of the complex formation, therefore, the ratio of bound water present in the hydrous gel was measured with DSC. Calculation results are shown in Figure 6 for the ratio of bound water inside the hydrous gel obtained with 30 minutes heating against the ratio of the same obtained with 1 minute hearing. The figures indicate an increase in the ratio of the bound water in the water inside the hydrous gel by heating, through the formation of interionic complexes. It has been also indicated that the increase is more prominent with higher concentration of the nonionic surfactant. The results have shown that in a zwitterionic polymer

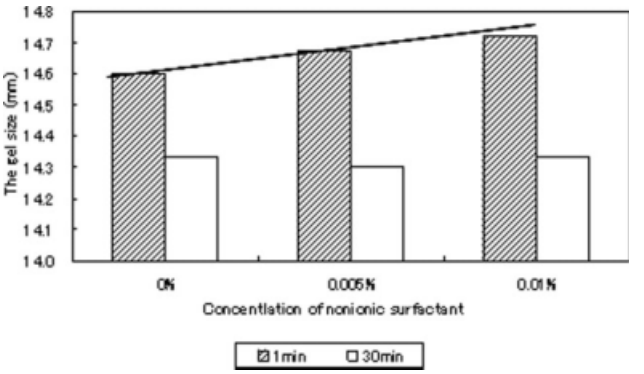

Figure 5 The relationship of the amount of nonionic surfactant added and the gel size at 1 minute and 30 minutes of heating.

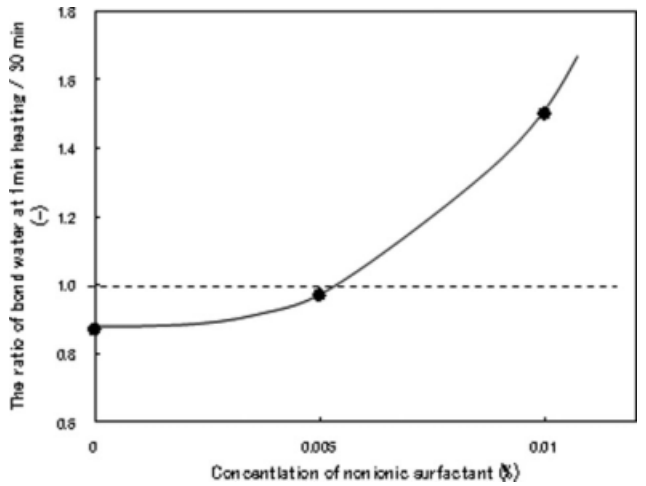

Figure 6 The ratio of bound water inside the hydrous gel obtained with 30 minutes heating against the ratio of the same obtained with 1 minute hearing.

gel, control of the state of water inside is possible, depending on time and environment of the heating.

For a polymer gel to be viable for practical use as a contact lens, beside safety, clarity, and sufficient strength are the requisites. The relationship of the heating time, at each concentration of the nonionic surfactant is shown in Figure 7(A) with stress and in (B) with flexure. At 1 minute heating, stress and flexure both declined with increasing concentration of the nonionic surfactant. And, at 30 minutes heating, stress and flexure both increased with the increase of concentration. Generally, it is known, strength of a polymer gel is governed by the density of crosslinking by covalent bonding, hydrophobic interactions among the sidechains, and electric interactions among ions. In the zwitterionic polymer gel in this study, variation in strength variation due to this electric interactions among ions is expected to be drastic. In 1 minute heating, therefore, as is indicated by the afore-mentioned results, stress and flexure both declined due to reduced complex formation with higher concentrations of the nonionic surfactant which hampered the ionic interactions among counterions in the hydrous gel. In 30 minutes heating on the other hand, it is estimated that prolonged heating intensified the complex formation among counterions. Farther, the increase in stress and flexure in line with the increase of the concentration of nonioninc surfactant may be caused by the interactions by the hydroxyl groups in the molecules of the nonionic surfactant, which was a higher alcohol, developed by the interionic complex formed while the nonionic surfactant was retained inside the hydrous gel.

Figure 8 shows the FTIR absorption spectra of the zwitterionic polymer gel before heating, after heating, and after heating with the nonionic surfactant. All of them have extra absorbance peak at approxi-

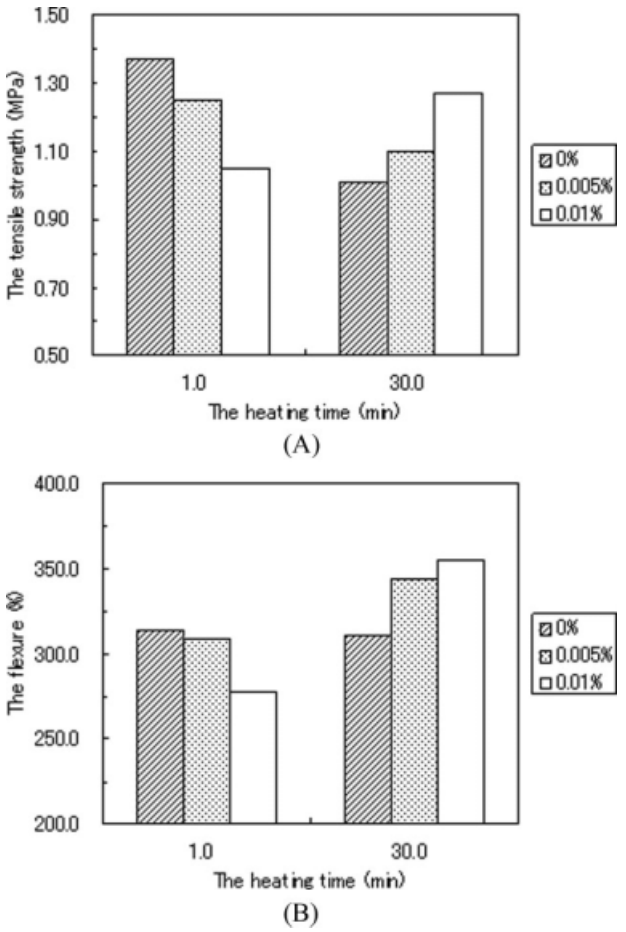

Figure 7 The relationship of the heating time, at each concentration of the nonionic surfactant with tensile strength (A) and with flexure (B). The quantities of nonionic surfactant added were 0, 0.005, and 0.01%.

mately in 1720 cm^{-1} from the carboxyl groups (—RCOO—, —COOH). In the both gels after heating with the nonionic surfactant and without one, the peak from the carboxylate anion (COO^-) appears in 1680 cm^{-1}. It indicates that the carboxyl groups

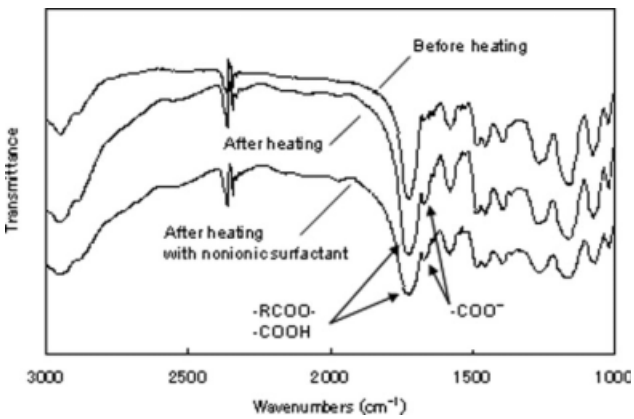

Figure 8 The FTIR spectra of a zwitterionic polymer gel. The samples ware before heating, after heating, and after heating with nonionic surfactant.

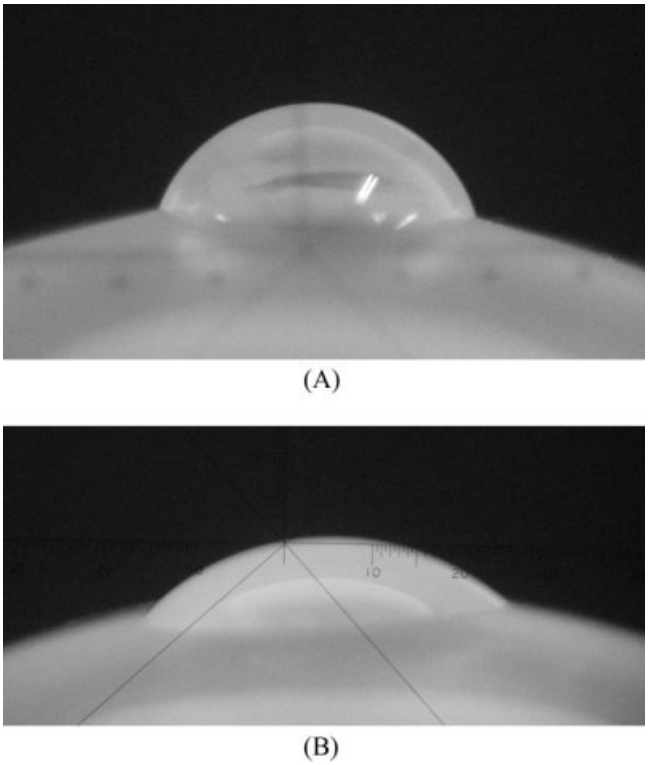

Figure 9 The contact angle of SCL using the zwitterionic polymer gel. (A) The SCL after heating without nonionic surfactant. (B) The SCL after heating with nonionic surfactant.

before heating exist undissociated, however after heating, the carboxylate anion is settled by ammonium ion, and the gel forms ion complex among counterions. In addition, this zwitterionic polymer gel is also formed in the presence of the nonionic surfactant because it doesn't block formation of ion complexs.

The contact angle of SCL using the zwitterionic polymer gel is shown Figure 9. In Figure 9(A) is the SCL heating in PBS and (B) is in PBS containing the nonionic surfactant. Although both SCL form ion complex, the SCL (B) is hydrophobic because of containing the nonionic surfactant. It indicates that the zwitterionic polymer gel could hold nonionic surfactant to have the high water retention capacity.

These results have demonstrated that, by heating a zwitterionic polymer gel in a solution containing the nonionic surfactant, formation of strong interactions between anionic and cationic groups inside the gel can be achieved. It has been also demonstrated that the ratio of bound water is increased within the gel, promising an enhanced strength. The suggested mechanism of these characteristics, as shown in Figure 3, is that the nonionic surfactant gets entangled with the interionic complex formed by the heating process and that affects the water retention capacity. The polymer gel in this study, when applied to a contact lens, may promise a practical realization of a novel type which can control evaporation of its own water, i.e., with a higher ratio of bound water, whereby providing a stable water retention.

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