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Evaluation of TRIS-DMA-NVP Hydrogels for Making Silicone-Based Contact Lenses

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***Abstract*—**In this study, contact lenses were prepared through the polymerization of tris-(trimethyl-silyl-propyl-methacrylate) (TRIS), N,N-dimethylacrylamide (DMA), N-vinylpyrrolidone (NVP), and cross-linked with ethylene glycol dimethylacrylate (EGDMA). The equilibrium water content (EWC), oxygen permeability (Dk), light transmittance, and *in vitro* cytotoxicity of TRIS-DMA-NVP with various ratios were measured. The results showed that the EWC increased while the Dk decreased with the increase of NVP content. For the sample with 25 wt% NVP, the EWC attained 53% whereas the Dk decreased to 46 barrers. All these lenses exhibited light transmittance over than 95%. In addition, all these lenses exhibited no inhibition to the growth of L292 fibroblasts. Thus, this study showed that TRIS-DMA-NVP can be applicable for making contact lens.

***Keywords*—**DMA, TRIS, NVP, silicone hydrogel, contact lens.

I. Introduction

OVER the past few decades, hydrogels are widely used to create soft contact lens because of properties including wearing comfort, physical and optical properties, and the improvement of water absorption [1]. Conventional hydrogel lenses were commonly made from hydrophilic monomers such as 2-hydroxyethyl methacrylate (HEMA), NVP, DMA, and glycerol methacrylate (GMA). Lai synthesized the soft lens from the incorporation of hydrophilic HEMA and NVP that showed a good EWC and more comfort during wearing time [2]. In other research, Garrett et al. exhibited that the combination of HEMA with different amounts of methacrylic acid (MAA) or NVP enhanced the water content and affected strongly the absorption of lysozyme and human serum albumin (HSA) [3]. Although hydrogel polymers obtained good characters under the open-eye conditions, the lenses still have an important drawback about the gas permeability. Because of the shortage of Dk, the hydrogel lens limits the oxygen supply for corneal epithelium during overnight wear. This problem leads to the corneal edema for patients who frequently wear contact lenses in the extended conditions [4], [5]. Moreover, with the high WC, the hydrogel lens will be easily broken and increase the protein absorption.

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Silicone can improve the Dk value of hydrogel lens due to silicon-oxygen bonds. Lai et al. reported that the incorporation of hydroxyl-terminated polydimethylsiloxane (PDMS) and HEMA provided more Dk than non-silicone hydrogel due to the reduction of water content [6]. In addition, Chekina et al. developed new contact lens from the copolymerization of oligosiloxane, DMA, and NVP. The results showed that the material possessed good mechanical character, light transmittance, oxygen, and water permeability [7]. Particularly, Lin et al. prepared the PDMS-PU-PEGMA silicone hydrogels from PDMS, isophorone diisocyanate (IPDI), HEMA, and poly(ethylene glycol) methacrylate (PEGMA). The hydrogels exhibited lower protein absorption, non-cytotoxicity, and high Dk as well as EWC [8].

TRIS is one of hydrophobic silicones to increase the ox Dk based on silicon-containing groups [9]. Besides, DMA and NVP were hydrophilic monomers containing hydrogen bonds [10]. In this study, TRIS was incorporated with DMA-NVP to improve the Dk and water content of hydrogel lens as well as other chemical and physical functions.

II. Experimental

A. Materials

TRIS, NVP, DMA, 2-hydroxy-2-methyl-1-phenyl-1-propanone (PI1173), EGDMA, dimethyl sulphoxide (DMSO), and lysozyme were purchased from Sigma-Aldrich, USA. HSA was purchased from Calbiochem, USA. Phosphate buffered saline solution (PBS, 0.1 M, pH 7.4) was prepared in our laboratory.

B. Preparation Silicone Hydrogels

The pre-hydrogel solutions were prepared by mixing TRIS, NVP and DMA according to the ratios in Table I. EGDMA and PI1173 were used as the cross-linker and photo initiator, respectively. For all the formulations, EGDMA and PI1173 were respectively added at 0.625 and 0.2 wt%. After stirred in dark at room temperature for 2 h, the mixtures were poured into contact lens' molds and cured under UV light (365 nm) at 5 mW/cm^2 for 30 min. The resultant hydrogels were immersed in 50% ethanol for 4 h at 70 °C to remove photo initiator and unreacted monomers. Then ethanol was removed by soaking in distilled water for 4 h at 70 °C. The obtained lenses were preserved in phosphate buffered saline (PBS, pH 7.4).

C. EWC

The dry samples were weighed after being dried in the oven at 40 °C for one day. Then, the specimens were soaked in distilled water at room temperature for one day [9]. The EWC of soft lens was calculated as follows:

$$EWC\ (\%) = \frac{W_2 - W_1}{W_2} \times 100 \quad (1)$$

where W_1 and W_2 are the weight of dry and wet hydrogel specimens.

D. Dk

The Dk was determined using an oxygen permeation apparatus (Model Dk-1000, Chiron Technology, USA). After fully swollen in distilled water, the center thickness of the lens was measured. Then the lens was put into the electrode and performed the polarography. The air humidity and temperature should be controlled at about 95% and 35 ± 5 °C, respectively. The Dk values were described in barriers [11].

E. Light Transmittance

The light transmittance of all samples was determined using a UV-Vis spectrophotometer (Cary 300, Agilient Technologies, USA). The specimens (1 cm × 3 cm) were placed in the cuvette in 2 ml of distilled water after soaked in the PBS solution. Then the spectra ranging 400-700 nm of the lens were scanned [12].

F. Protein Adsorption

The hydrogel lenses (1 cm × 1 cm) were incubated for 24 h at 37 °C after placing in 1 ml PBS containing 2 mg HSA or lysozyme. The samples were taken out and cleaned 5 times with PBS. After that, the specimens were soaked in 2 ml sodium dodecyl sulfate (SDS) and then were put in the ultrasonic bath for 60 min at 37 °C. Then, the samples were added into 2 ml bicinchoninic acid (BCA) and shaken in incubator for 60 min at 37 °C. The protein adsorption of these samples was measured at 562 nm using a UV-Vis spectrometer.

G. Cell Toxicity

The *in vitro* cytotoxicity of the soft lens was carried out according to ISO 10995-5. The culture medium contained 1% penicillin (PNC), 5% fetal bovine serum (FBS), and 94% Dulbecco's Modified Eagle's medium (DMEM). The lenses of 1 cm × 1 cm were put in UV room for 4 h and then were incubated in the medium for one day at 37 °C. Then the extract medium was sterilized with 0.22 µm filter. The L929 cell culture medium was transferred to the flask and then cultured for two days at 37 °C. Afterwards, the MTT reagent and DMSO were sequentially added into the flask with specimen. The cell toxicity was determined based on the absorbance at 570 nm. The positive control was developed to compare with the negative control [8].

III. Results and Discussion

A. EWC

In this study, all formulas consisted hydrophobic TRIS and hydrophilic DMA-NVP. As shown in Table I, the water content of silicone hydrogel was depended on the NVP content. The EWC increased from 43% to 52.8% when the NVP content increased from 0 to 25 wt%. As shown in Fig. 1, NVP is polar and can form hydrogen bonds with two water molecules [16], [17]. Moreover, DMA is also hydrophilic, conferring high EWC at 0% NVP content [10]. Therefore, the presence of DMA and NVP monomers led to the water absorptibility in silicone hydrogel matrix.

TABLE I
THE WATER CONTENT AND DK OF TRIS-DMA-NVP HYDROGEL

Sample	Ratio (wt%)			EWC (%)	Dk Value (barrers)
	TRIS	DMA	NVP		
1	50	50	0	42.9 ± 1.0	52
2	46.15	46.15	7.7	48.5 ±0.1	51
3	42.86	42.86	14.28	49.1 ± 0.9	49
4	40	40	20	50.7 ± 0.3	48
5	37.5	37.5	25	52.8 ±1.5	46

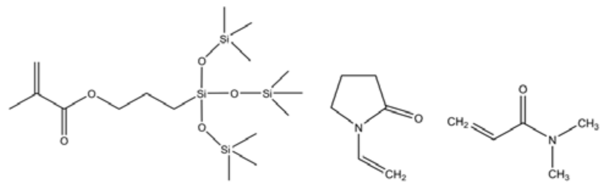

Fig. 1 The structure of TRIS, DMA and (NVP) for silicone hydrogels

Zhao et al. reported that the EWC increased with the NVP in the polymerization of bis(trimethylsilyloxy) methylsilylpropyl glycerol methacrylate (SiMA), HEMA, NVP, and DMA [18]. Wang et al. indicated that for the interpenetrating polymer network (IPN) of siloxane macromer/TRIS/DMA/NVP, the EWC increased with NVP content. At the same ratio of siloxane macromer, TRIS, and DMA, the EWC attained 63% when the NVP content was 50 wt% [19]. In this work, the presence of DMA and NVP monomers increased the water absorption ability in silicone hydrogel matrix.

B. Dk

The Dk is one of the most significant indexes that dominate the oxygen supplement and wearing comfort of the eyes [20]. In general, the water content and Dk are in the inverse relationship in silicone hydrogel network. Contrastively, EWC is the main trouble to concern to the decrease of Dk value [21]. In this work, when the EWC increased from 42.9 to 52.8%, the Dk decreased slowly from 52 to 46 barrers. This downward tendency can be attributed to the decreased TRIS concentration in hydrogel matrix. Hydrophobic TRIS with the Si–$(CH_3)_2$–O side group containing four silicone atoms in monomer structure can enhance the oxygen absorptivity through the interaction of silicon-oxygen bond (Fig. 1). Besides, the flexible TRIS in matrix caused the phase separation including hydrogel continuous phase and silicone phase [11]. Hence, the oxygen can pass easily through hydrogel lens to reach the corneal epithelium. Thus TRIS can improve the Dk for contact lenses.

Wang et al. used TRIS, HEMA, and NVP and showed the amelioration of Dk value corresponding to the ratio change of TRIS from 10 to 30 wt%. The highest Dk of 72.3 barrers was attained at 30% TRIS [22]. Similarly, Zhao et al. synthesized silicone hydrogels with different ratios of SiMA, TRIS, HEMA, DMA, and NVP. At the TRIS content of 30 wt%, the highest Dk of 29.6 barrers was attained [11]. Therefore, this study is in accordance with the result of other researches.

C. Light Transmittance

Fig. 2 shows the light transmittance of all samples were above 95%. The light transmittance of a hydrogel lens should be more than 90% in the wavelength range of 400-700 nm [23]. Thus, in this study, all of TRIS-DMA-NVP polymers were feasible for contact lens application.

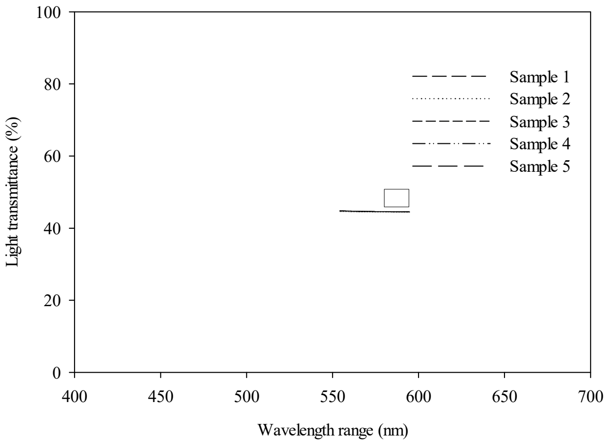

Fig. 2 The light transmittance of TRIS-DMA-NPV silicone hydrogels

D. Protein Adsorption

Fig. 3 displays the protein adsorption of silicone hydrogel samples by measuring HSA and lysozyme deposits following a BCA assay. The protein deposition of all samples enhanced with the increasing of NVP content corresponding to the reducing of TRIS amount. The maximum values of HSA and lysozyme attained respectively at 5.15 µg/cm^2 and 2.76 µg/cm^2 with the highest percent of NVP (25 wt%). This means that NVP is obviously a factor to enhance the protein adsorbability on the surface of lens samples. With lens materials, the high deposition of protein may cause wearing discomfort, limiting vision correction and enhancing the attached risk of microbial cells [24].

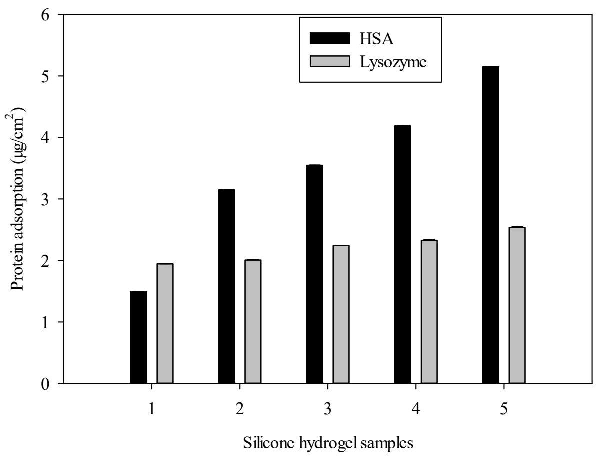

Fig. 3 Protein adsorption of silicone hydrogel samples

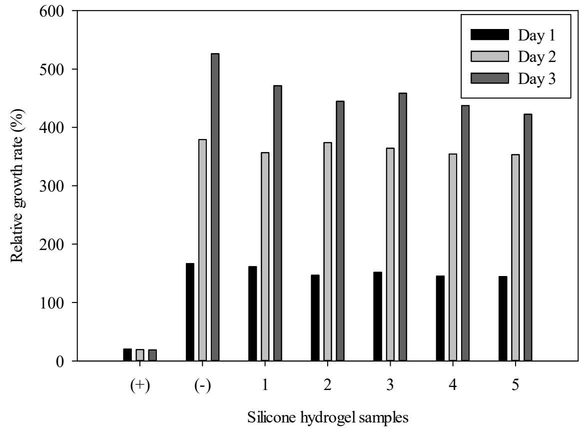

Fig. 4 Relative growth rate of TRIS-DMA-NPV silicone hydrogels during 3 cultured days with (+) positives control, (-) negative control, (1, 2, 3, 4, 5) L929 cells of TRIS-DMA-NVP samples

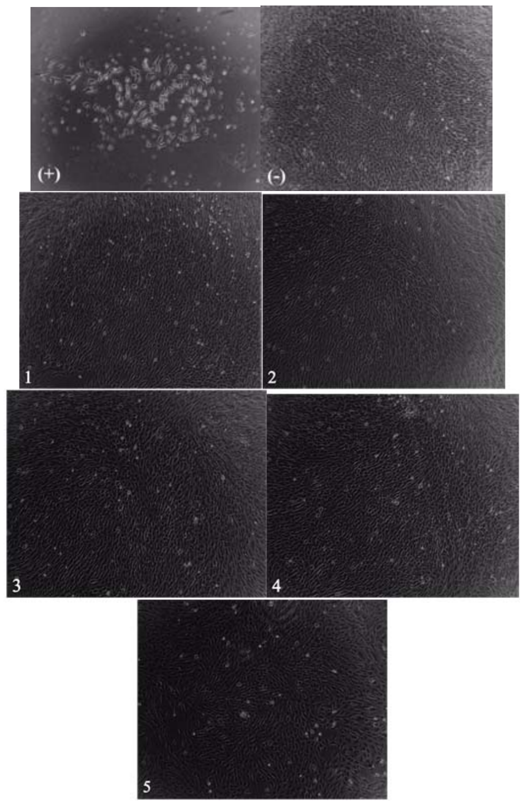

Fig. 5 The growth of L929 cell incubated with extracted medium after 3 days

E. Cell Toxicity

The *in vitro* cytotoxicity test is for evaluating the toxicity of the material to cellular growth based on the change of biological morphology. Wang et al. showed that the incorporation of cationic photo initiator and TRIS-HEMA-NVP led to cellular death [9].

Fig. 4 shows the cytotoxicity test of the extract medium of hydrogel lens. The RGR value increased from day 1 to day 3 for all extracted media. Moreover, in Fig. 5, all of silicone hydrogel specimens appeared non-cytotoxic with cells. Hence, this result indicated that the combination of TRIS-DMA-NVP and PI1173 was non-toxic to L929 cells.

IV. Summary and Conclusions

The various ratios of TRIP-DMA-NPV were used to synthesize silicone hydrogel lens by exposure to ultraviolet (UV) light. The various NVP content strongly affected the water content and Dk in silicone hydrogel matrix. The best sample in this study exhibited a Dk value of 52 barrer and EWC value of 46% with the light transmittance over 95%.

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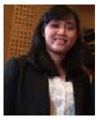

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