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Thermally Crosslinked Biocompatible Hydrophilic Polyvinylpyrrolidone Coatings on Polypropylene with Enhanced Mechanical and Adhesion Properties

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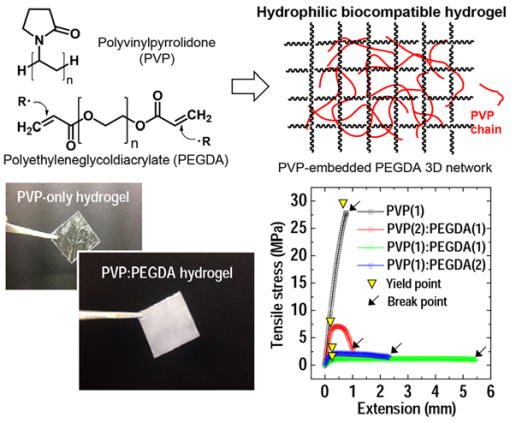
Abstract: We developed a stable hydrophilic biocompatible hydrogel-forming coating for polypropylene (PP)-based disposal medical applications. Although PP has a variety of advantages, including good stability and inertness in medical applications, tissue damage and insertion resistance are observed upon insertion of PP-based devices into the human body due to the high hydrophobicity of the PP surface. These issues limit the utility of PP in medical applications. To address these problems, we sought to develop a stable hydrophilic and biocompatible hydrogel-forming layer using polyvinyl pyrrolidone (PVP) combined with a crosslinked polyethyleneglycolacrylate (PEGDA) matrix. Systematic studies of the blended hydrogel-forming PVP:PEGDA were conducted using a variety of blending ratios between the two polymers. The hydrophilicity and water-affinity of the hydrogel-forming layer improved significantly as the PEGDA-to-PVP blending ratio increased. Importantly, the tensile strain at the break point increased by a factor of more than 7, and the strength of adhesion to the PP surface for the 1:1 PVP:PEGDA (PVP(1):PEGDA(1)) blend ratio was 54 times that of the PVP film, determined using tensile strain–stress and peel tests. The water stability of the PVP(1):PEGDA(1) improved significantly. This approach is potentially useful as a biocompatible hydrophilic polymer coating in a variety of low-priced consumable PP commercial medical applications.



Keywords: polyvinylpyrrolidone, biocompatible hydrogel, hydrophilic coating, polypropylene, adhesion, polyethyleneglycolacrylate.

1. Introduction

Over the past few decades, advances in polymer materials have spurred the development of disposable medical applications, such as catheters,[1-3] ophthalmic cartridges,[4,5] and guidewires.[1,6,7] Many novel polymers have been designed and fabricated to fulfill the ever-increasing needs of the medical field.[8-12] Polyamide, polyacetal, fluorocarbon, polyether block amide, and polyurethane are commonly used as non-degradable medical polymers. Relatively high material costs have driven efforts to replace these polymers with polypropylene (PP), which is an inexpensive inert material.[13,14] PP-based medical devices that are inserted into the human body suffer from insertion fatigue, and the high hydrophobicity of the PP surface renders the devices non-biocompatible, producing side effects, such as tissue damage and pain upon insertion.[15] These problems may be addressed by developing hydrophilic biocompatible polymer coatings for use in PP-based medical applications.

Hydrogel films typically directly contact biological tissues in medical applications; thus, biocompatibility and non-toxicity are two major considerations for hydrogel films.[16-19] Polyvinyl pyrrolidone (PVP) is a biocompatible polymer that can form a hydrogel.[20-22] It is used in a variety of medical, food, and cosmetic applications as a film-forming agent; however, PVP-based films are not stable in water, and they have a low mechanical strength, rendering them unsuitable as coating materials for medical polymer applications.[20,22] PVP films are easily peeled off of surfaces because PP has low surface adhesion properties resulting from a high surface hydrophobicity. Plasma or ultraviolet-ozone treatments are commonly used to increase the adhesion properties of the coating film by imparting hydrophilicity to the surface of the polymer; however, these treatments do not significantly alter the PP material chains given that the stable main chains of PP consist of methylene groups.[23,24] Other approaches are needed to address these problems.

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In this study, we sought to stabilize PVP film coatings using a crosslinked matrix composed of polyethyleneglycolacrylate (PEGDA). PEGDA is a biocompatible polymer that can form crosslinks that increase the film strength.[18-20] The formation of hydrogen bonds between PEGDA and PVP chains can prevent film dissolution in water and improve certain desirable mechanical properties, such as the degree of elongation at break, adhesiveness, and toughness. We found that the mechanical strength and water stability of a PVP:PEGDA polymer coated onto a PP surface depended on the PVP and PEGDA blend ratio. A 1:1 blend ratio provided the best characteristics in terms of the mechanical strength, water stability, and adhesion properties of the highly hydrophobic PP surface. Increasing PEGDA in the hydrogel-forming matrix decreased the water contact angle, which is somewhat related to the lubricious properties, and increased the degree of water absorption into the hydrogel-forming matrix. These results further the development of biocompatible, hydrophilic polymer coatings for use in low-priced consumable PP medical products.

2. Experimental

2.1. Materials

Polyvinylpyrrolidone (PVP, M_w=360 k) and poly(ethylene glycol) diacrylate (PEGDA, M_w=302) were purchased from Tokyo Chemical Industry Co. Benzoyl peroxide (BPO) was purchased from Sigma-Aldrich Co. Ethanol was used to dissolve PVP and PEGDA. Toluene was used as a solvent of BPO. 95% ethanol denatured with 5% methanol and 99.5% toluene were purchased from Samchun Pure Chemical Co., Ltd. All chemicals purchased in this study were used without additional purification. Ultrapure deionized water was used to evaluate the water stability of the hydrogel-forming films.

2.2. Fabrication of the hydrogel-forming films

PVP and PEGDA were dissolved in ethanol and stirred at 60 °C. PVP was dissolved in 25 wt% ethanol, and PEGDA was added in various ratios relative to the concentration of PVP. In our experiment, the PEGDA ratios were 50, 100, and 200 wt%, referred to as PVP(2):PEGDA(1), PVP(1):PEGDA(1), PVP(1):PEGDA(2), respectively. The PVP:PEGDA solutions were stored for 1 h under ambient conditions to permit the temperature to equilibrate, and BPO was added in an amount equal to 1 wt% of PEGDA. PVP:PEGDA solutions prepared with various blended ratios were poured into a petri dish to fabricate own films or coated onto a PP film. These samples were dried at room temperature for 6 h. The dried PVP:PEGDA films were heated in an oven at 60 °C for 30 min to initiate the thermal crosslinking reaction with BPO, the thermal initiator. The films were stored in a vacuum desiccator.

2.3. Characterization

Water contents (wt%) of PVP and hydrogel-forming PVP:PEGDA prepared by the above procedure were measured by a weight change after the complete drying at 120 °C for more than 2 days. The water content ratio in the coated hydrogels were 11.9, 18.1, 23.7, and 22.9 wt% in the PVP, PVP(2):PEGDA(1), PVP(1):PEGDA(1), and PVP(1):PEGDA(2) cases, respectively. The morphologies of the hydrogel-forming films were characterized using a photographic camera, optical microscope (Eclipse 80i, Nikon), and field-emission scanning electron microscope (SEM, Hitachi S-4200). The hydrophilic properties of the various hydrogel-forming films were characterized by measuring the water contact angle using a contact angle analyzer (Phoenix 300A, SEO Co., Inc.) as a function of time under ambient conditions below 15 °C. The used water droplet size was 10±0.5 μL, which was automatically controlled by the measuring equipment. of Tensile stress-strain and peel tests were conducted using a micro-material tester (Instron 5848). The PVP and hydrogel-forming PVP:PEGDA films used in the tensile stress-strain test were 15 mm long, 0.6-1.8 mm thick, and 9-12 mm wide. The thickness and width were calculated based on the measured values. The crosshead of the micro-material tester was moved at a speed of 1.5 mm/min in intervals of 0.5 s. The samples used in the peel test were prepared by coating PVP and hydrogel-forming PVP:PEGDA films onto PP surfaces in a width of 20 mm. The peel tests were performed at an angle of 180°.

3. Results and discussion

Figure 1(a) shows the chemical structures of PVP as a hydrophilic polymer, PEGDA, which formed a polymer matrix, and the benzoyl peroxide (BPO). Figure 1(b) shows a schematic diagram of the mechanism by which the polymer matrix formed. BPO, a thermal initiator, decomposed between 60 and 80 °C and produced active radicals that reacted with the vinyl groups in the PEGDA chain to induce migration of the radicals to the PEGDA chains.[25,26] The PEGDA radicals reacted continuously with the vinyl groups of other PEGDA to form a crosslinked polymer matrix.[20,25] As for PVP, following the crosslinking reac-

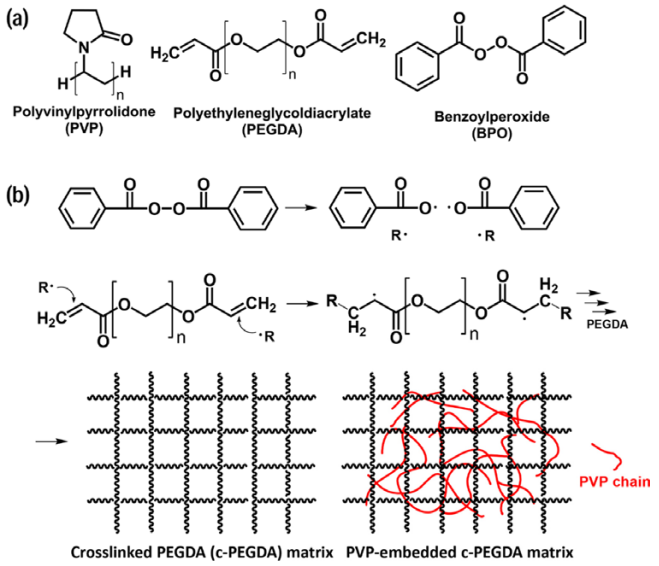

Figure 1. (a) Chemical structures of PVP, PEGDA, and BPO used in this system. (b) Schematic diagrams of the PEGDA crosslinking mechanism and the PVP-embedded c-PEGDA matrix.

tion of the PEGDA they get entrapped in the PEGDA 3D hydrogel-forming matrix. In additional, the PEGDA and embedded PVP chains could be physically crosslinked between hydroxyl/carbonyl and amide/carbonyl groups in the PEGDA and PVP molecules, respectively, which can lead to the formation of hydrogen bonding networks. Therefore, an PVP-embedded PEGDA hydrogel-forming matrix will form, composed of 3D crosslinked PEGDA network with covalent bonding and linear PVP polymer chain entrapped in the 3D network, resulting in stable PVP:PEGDA hydrogel-forming films.[20,27] In this experiment, the PEGDA blend ratio was set to 50, 100, and 200 wt% based on PVP in an effort to optimize the crosslinked hydrogel-forming blend conditions, referred to as PVP(2): PEGDA(1), PVP(1):PEGDA(1), PVP(1):PEGDA(2), respectively.

Figure 2 shows photographs and SEM images of PVP:PEGDA hydrogel-forming films prepared with 650±60 μm, with various PVP and PEGDA blend ratios. The PVP film prepared without PEGDA was transparent, and featured a line structure within the film, as shown in the photograph and SEM image. The line structures may have formed during the PVP film fabrication process, rather than reflecting an intrinsic material property. Such structures are typical of shrinkage upon PVP solution drying.[28] The addition of PEGDA to PVP produced opaque films, regardless of the PEGDA ratio, as shown in the photographs. As the PVP:PEGDA blend ratio was varied, the surface morphologies shown in the SEM images varied. The surface of the hydrophilic films prepared with the PVP(2):PEGDA(1) blend ratio formed a concavo-convex structure, whereas the surfaces of the other blended films were relatively flat. The concavo-convex structures generally occurred when the two materials were phase-separated.[29,30] The polymer blend theory suggested that the PVP molecules were not effectively stabilized by the PEGDA matrix and formed phase-separated domains on the film surface if an insufficient quantity of the PEGDA matrix were present compared to the PVP.[20,22] As the PEGDA blend ratio increased, for example, in PVP(1):PEGDA(1) and PVP(1):PEGDA(2), the their surfaces were flat and uniform, indicating that the PVP molecules were uniformly stabilized and dispersed throughout the PEGDA matrix, as described above. The PVP(1):PEGDA(1) surface was the smoothest surface prepared here, as shown in the SEM images. This ratio was expected to provide a hydrogel-forming film with the best blending characteristics and mechanical properties.

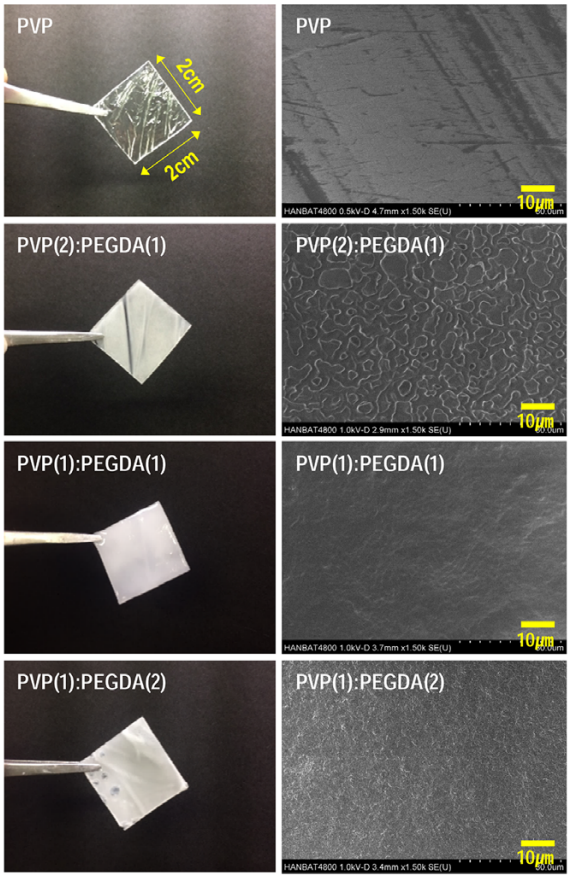

Figure 2. Photographs (left) and SEM images (right) of hydrophilic hydrogel-forming films prepared with various PVP:PEGDA ratios.

Figure 3 shows a graph of the water contact angle variations over time. To minimize the problems of droplet size change due to the water evaporation, these measurements were carried out under low temperature conditions lower than 15 °C. CCD images of the initial water contact angles showed the hydrophilicity of the PVP film and the various PVP:PEGDA hydrogel-forming films coated on the PP surface. The contact angle is an important factor that determines the insertion characteristics of consumable medical devices and can predict the friction characteristics and the degree of tissue damage incurred during insertion.[8,31] PP polymer films used in low-cost consumable medical devices displayed an initial contact angle of 79° and a relatively high hydrophobicity. The contact angles did not change significantly over 30 min. The initial contact angle of a water droplet on the PVP film, a biocompatible polymer, was found to be 43°, indicating a low hydrophilicity. The contact angle decreased over time, and the droplet was undetectable on the PVP film surface after about 15 min. The water droplets used to measure the contact angle were not lost to evaporation, but were absorbed into the PVP film, which could dissolve in water due to the high water solubility of the PVP. As the

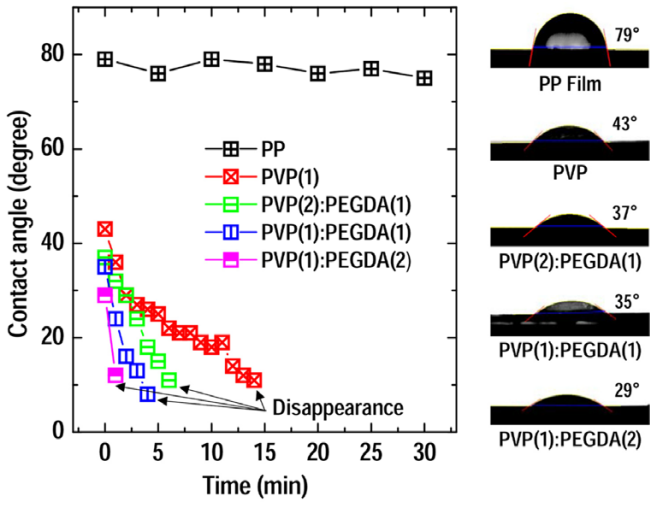

Figure 3. Water contact angle variations on the various films as a function of time, and CCD images of the initial contact angles after dropping the water droplets.

PEGDA content in the hydrogel-forming film increased, the initial contact angle decreased from 37° on PVP(2): PEGDA(1) to 29° on PVP(1):PEGDA(2). Particularly, the noteworthy point is the time at which the water drops disappeared from the surface. The disappearing times shortened dramatically as the PEGDA content increased, from 6 min for PVP(2):PEGDA(1) to 4 and 1 min for PVP(1):PEGDA(1) and PVP(1):PEGDA(2), respectively. The numerous oxygen atoms in the PEGDA chains formed hydrogen bonds with water and increased water absorption into PEGDA.[32] As the PEGDA content increased, the time at which the water droplet on the PVP:PEGDA film disappeared was shortened.

The tensile stress-strain and peel tests were conducted to evaluate the mechanical properties of the PVP:PEGDA blended hydrogel-forming filmss developed in this study. Figure 4(a) shows a diagram of the tensile stress-strain test results obtained from the PVP:PEGDA blended films, and the results are summarized in Table 1. As shown in the Table, the modulus of the PVP-only film yielded the highest hardness of 489.72 MPa, and the hardness decreased as the PEGDA blend ratio increased, providing the lowest value of 52.28 MPa in the PVP(1):PEGDA(1) film. The hardness value increased to 115.11 MPa despite a PEGDA ratio increased in the case of the PVP(1):PEGDA(2) film. The intrinsic hardness of the crosslinked PEGDA matrix may have been reflected in the results because the blend ratio of the crosslinkable PEGDA was much higher than that of PVP.[22,33] Figure 4(a) and Table 1 present the tensile strains at the break points. PVP displayed the highest modulus due to a strong hardness, but PVP was easily broken, with a tensile strain of 7.66% at the break point. On the other hand, the PVP:PEGDA blend films showed higher tensile strains at the break points compared to the PVP-only case, particularly the PVP(1):PEGDA(1) case, which had a tensile strain of 54.53% at the break point. These results revealed that the PVP:PEGDA hydrogel-forming films were more flexible and strong with the addition of PEGDA, despite a decrease in the film hardness.[21,34] Flexible strong films are important among biocompatible hydrophilic coating to disposable medical devices inserted into the human body because these properties ensure smooth insertion without tissue damage.[9,11] In other words, PVP(1):PEGDA(1) exhibited physical properties that were suitable for use as a hydrogel-foming polymer coating in disposal medical applications. PEGDA contents that are significantly higher than the PVP content, as in the PVP(1):PEGDA(2) case, yielded lower tensile strains at the break point, 23.11%. These results presumably arose from reduced flexibility and extensionality due to greater crosslinking within the PEGDA matrix.

Figure 4(b) shows the peel test results obtained from various hydrogel-forming films coated on a PP film. The PVP-only coating on the PP film provided a first maximum peak at a peel strength of 0.01 N with a displacement of 0.5 mm. The average peel strength displayed a low adhesive strength of 0.04 N. On the other hand, the peel strength tended to increase with the addition of PEGDA.[20,35,36] The first maximum and the average strengths of the PVP(1):PEGDA(1) case were 0.54 and 0.21 N, respectively, a much greater adhesive strength compared to the PVP-only case. The formation of a hydrogel-forming film from a PEGDA matrix crosslinked with PVP chains decreased the hardness and increased the flexibility/strength of the film, as shown in Figure 4(a), thereby improving the adhesion properties. Molecular entanglement during thermal crosslinking of the PEGDA matrix on the PP surface could be expected to improve the surface adhesion properties; however, an excess of PEGDA in the PEGDA:PVP blend ratio decreased the peel strength, as discussed above, due to an increase in the hardness and PEGDA intermolecular bonds in the presence of a high crosslinkable PEGDA content.

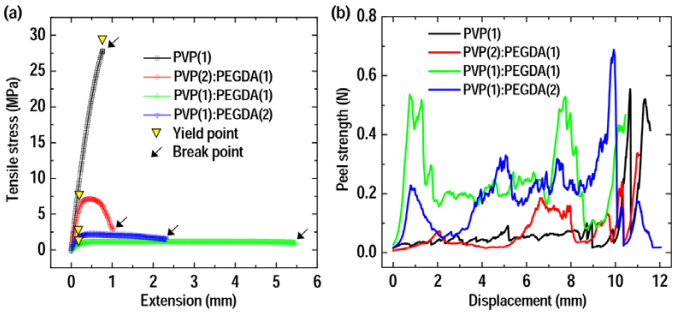

Figure 4. (a) Tensile stress-strain diagrams of various hydrophilic hydrogel-forming films used in this study. (b) Measured peel test results obtained from various hydrophilic hydrogel-forming films peeled from a PP surface.

Figure 5 shows the film changes during water immersion for 60 min to compare the water stability of the PVP and PVP:PEGDA blend hydrogel-forming films prepared in this study. The PVP film dissolved slowly immediately after immersion into water.[22,34,37] The film became translucent after 20 min and was not observable after 30 min. The film eventually dissolved completely in water, and no traces were found after 60 min. The PVP(2):PEGDA(1) film became damaged after 10 min. The film was shown to dissolve gradually over 30 min, and the film shape was unobservable after 60 min, despite the film's persistence. The PVP-only and PVP:PEGDA films displayed slightly different water damage effects.[38] The PVP-only film dissolved in water, and its shape deformed, but the PVP:PEGDA blended films deformed as if the films had been broken. Distinct deformation properties were observed in the PVP(1):PEGDA(1) and PVP(1):PEGDA(2) cases, in which the PEGDA blend ratio was high. The hydrogel-

Table 1. Summaries of the tensile stress-strain diagram

Sample	Maximum Load (N)	Tensile stress at Maximum Load (MPa)	Tensile strain at Maximum Load (%)	Extension at Break (mm)	Tensile strain at Break (%)	Modulus (MPa)
PVP	160.07	27.79	7.66	0.77	7.66	489.72
PVP(2):PEGDA(1)	47.01	7.12	4.49	1.02	10.24	351.60
PVP(1):PEGDA(1)	24.48	1.11	27.24	5.45	54.53	52.28
PVP(1):PEGDA(2)	27.82	2.24	4.99	2.31	23.11	115.11

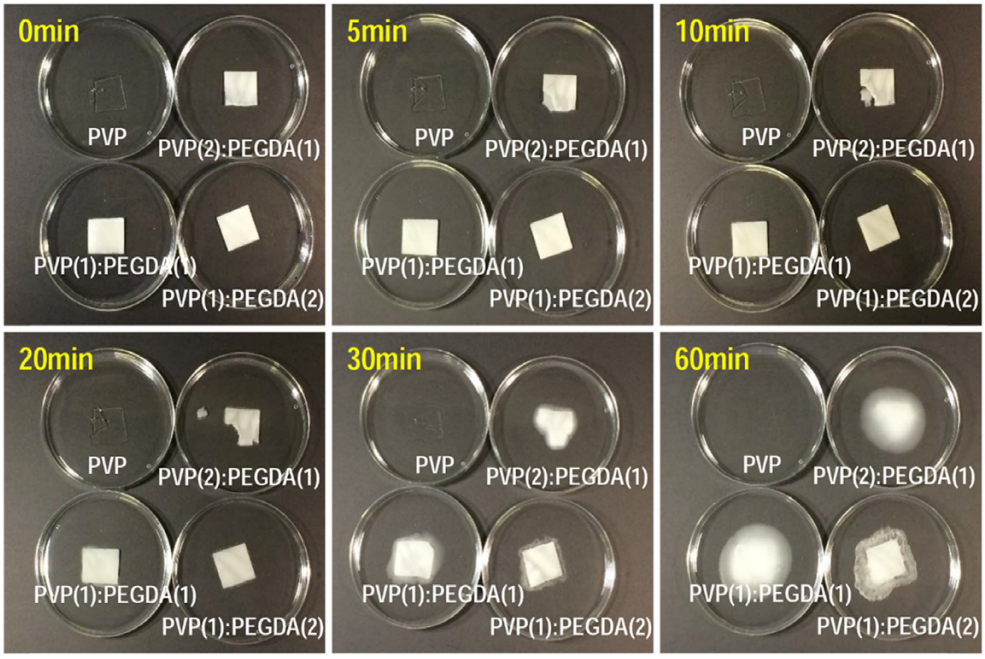

Figure 5. Photographs of the stability tests of PVP-only and PVP:PEGDA films in water over 60 min.

forming matrix may have collapsed upon dissolution of the PVP molecules from the crosslinked PEGDA matrix. As the PEGDA mixing ratio increased, the water stability increased. The PVP(1):PEGDA(1) film decomposed after 20 min, although the shape was maintained. Consumable insertable medical devices tend to remain in the human body for only a short time; therefore, hydrophilic and biocompatible hydrogel-forming films that remain stable for 20 min may be sufficient for commercial product applications.

4. Conclusions

In summary, we developed a stable hydrophilic and biocompatible polymer coating for use on a PP-based disposal medical device. PP is a commercial polymer commonly used in low-cost polymer medical applications. The highly hydrophobic PP surface can cause tissue damage or resistance during insertion into the human body, which limits its utility. These problems may be addressed by introducing a stable hydrogel-forming coating based on a PVP film crosslinked with PEGDA. Systematic studies of the hydrogel polymer blends comprising PVP and PEGDA revealed the mechanical properties and water stabilities of the films. The films' surface adhesion to the PP surface was analyzed as a function of the polymer blend ratio. The hydrophilicity of the hydrogel-forming films improved, and the time required by the film to absorb moisture decreased as the PEGDA to PVP blend ratio increased. The mechanical strength of the hydrogel-forming film and the adhesive force on the PP surface were found to be optimal for PVP(1):PEGDA(1). Importantly, the tensile strain at the break point increased by a factor of 7, and the adhesion strength to the PP surface increased by a factor of 54 compared with the PVP-only film. The water stability of the PVP(1):PEGDA(1) film was significantly better than the water stabilities of the other films tested. These results supported the use of a biocompatible hydrophilic polymer coating on low-cost consumable PP medical products.

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