Preparation and Characterization by Radiation of Hydrogels of PVA and PVP Containing *Aloe Vera*

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ABSTRACT: In these studies, hydrogels for wound dressing were made from a mixture of *Aloe vera*, poly(vinyl alcohol) (PVA) and poly(*N*-vinylpyrrolidone) (PVP) by freeze-thaw, gamma-ray irradiation, or a two-step process of freeze-thaw and gamma-ray irradiation. Physical properties, such as gelation, water absorptivity, gel strength and degree of water evaporation were examined to evaluate the applicability of these hydrogels to wound dressing. The PVA:PVP ratio was 6:4, and the dry weight of *Aloe vera* was in the range of 0.4-1.2 wt %. The solid concentration of PVA/PVP/*Aloe vera* solution was 15 wt %. Mixtures of PVA/PVP/*Aloe vera* were exposed to gamma irradiation doses of 25, 35 and 50 kGy to evaluate the effect of irradiation dose on the physical properties of the hydrogels. Gel content and gel strength increased as the concentration of *Aloe vera* in PVA/PVP/*Aloe vera* decreased and as irradiation dose increased and freeze-thaw was repeated. Swelling degree was inversely proportional to gel content and gel strength. © 2003 Wiley Periodicals, Inc. J Appl Polym Sci 91: 1612–1618, 2004

Key words: hydrogels; gels; radiation; hydrophilic polymers; crosslinking

INTRODUCTION

Hydrogels are most often defined as two-component systems in which one of the components is a hydrophilic polymer, insoluble in water because of a three-dimensional network joined as chains, and the other component is water. These systems may swell in water up to an equilibrium state and retain their original shape. The interactions responsible for water sorption by hydrogels include the processes of hydration, which is connected to the presence of such chemical groups as -OH, -COOH, -$CONH_2$, -CONH-, -SO_3H, and to the existence of capillary areas and differences in osmotic pressure. The forces that make hydrogel dissolution impossible are connected to the existence of covalent bonds between individual polymer chains, although they may also be electrostatic or hydrophobic in character.

The use of hydrogels to replace damaged tissues has been the main incentive for their synthesis and detailed investigation. The polymer gels have a very low modulus of elasticity, and therefore cause minimal mechanical irritation. They are chemically stable in a living environment, and permeable to low molecular weight metabolites, which are formed at the boundary between the living and non-living tissue. Thus, they moderate the physical abnormality of the boundary. They usually show good biocompatibility in contact with blood, body fluids and tissues.[1] In recent years, much attention has been focused on the research and development of polymer hydrogels for biomaterials, such as contact lenses, wound dressing, enzyme immunoassays, catheters and drug delivery systems.[2]

Hydrogels may be classified as homopolymer hydrogels, copolymer hydrogels, multipolymer hydrogels or interpenetrating polymeric hydrogels. Homopolymer hydrogels are crosslinked networks of one type of hydrophilic monomer unit, whereas copolymer hydrogels are produced by the crosslinking of two comonomer units, one of which must be hydrophilic. Multipolymer hydrogels are produced by the crosslinking of more than three monomers. Finally, interpenetrating polymeric hydrogels are produced by first swelling a network in a monomer and then reacting the latter to form a second intermeshing network structure.[3] Copolymer hydrogels or multipolymer hydrogels make them attractive because they impart a variety of the chemical and physical properties for medical applications by combining the different monomeric units.

Natural polymers such as chitin, chitosan, alginate, and *Aloe vera* have been used on wounds because they play an important role in the healing process. However, natural polymers have been considered limited in their applications as wound dressing materials because of their shortage of mechanical properties. The combination of natural and synthetic polymers can endow optimal properties for wound repair.

Aloe vera is a member of the Liliaceae family. The parenchymal tissue of *Aloe vera* leaves contains over 98≈99% water, and more than 60% of the dry matter

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is made up of polysaccharides.[4] The fresh leaves of *Aloe vera* are used to obtain two components: (1) a bitter yellow juice (exudate) with a high content of 1,8-dihydroxyanthraquinone derivatives (*Aloe vera* emodin) and their glycosides (aloins), which are used for their cathartic effects, and (2) a mucilaginous gel from the parenchymal tissue, which is used for the topical treatment of skin burns and wounds.[5] *Aloe vera* is employed in a host of curative purposes, including treatment of skin disorders and healing of burns and wounds. The fresh gel, juice or formulated products is used for medical and cosmetic purposes, as well as for general health. In spite of its wide use as a folk remedy, the biochemical basis of its action or its influence on the various phases of wound healing has not been studied in detail.[6]

Poly(vinyl acetate (PVA) has been frequently used in the preparation of various membranes and hydrogels.[7] Poly(*N*-vinyl pyrrolidone) (PVP) hydrogel has excellent transparency and biocompatibility. PVP has been used as a main component in temporary skin covers or wound dressings.[8]

Irradiation has been recognized as a highly suitable tool to aid in the formation of hydrogels. The radiation process has various advantages, such as easy process control, the possibility of joining hydrogel formation and sterilization in one technological step, the lack of necessity for initiators and crosslinkers, which are possibly harmful and difficult to remove. These qualities make irradiation the method of choice in the synthesis of hydrogels.[9]

In this work, we attempted to prepare hydrogels for wound dressing that consist of PVA, PVP, and *Aloe vera*. The physical properties, such as gelation, swelling, gel strength, and degree of water evaporation, were examined to evaluate the usefulness of hydrogels for wound dressing. The PVA/PVP/*Aloe vera* hydrogels were used in healing tests on rats.

EXPERIMENTAL

Materials

PVP (average $M_w = 1.3 \times 10^6$) and PVA (average $M_w = 8.5 \times 10^4 \approx 1.46 \times 10^5$) were supplied by Aldrich Chemical Company (Milwaukee, WI). Fresh *Aloe vera* (*Aloe vera* barbadensis Miller) plant was obtained from a farm in Korea. Distilled water was used as a solvent in all experiments.

Preparation of hydrogels

The *Aloe vera* leaf consists of three layers. The first is a thick cuter green rind. The second is a viscous, jelly-like mucilate layer that contains vascular bundles, which are attached to the inner surface of the rind. The third is the fillet proper, which has a structural integrity consisting of hexagonal structures containing the fillet fluid. The fillet, with 98% water content, was harvested from the green leaves, ground in a crusher, and homogenized.

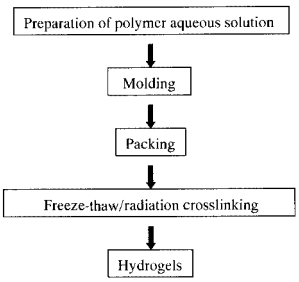

Figure 1 Flow chart for the preparation of hydrogels by radiation crosslinking.

PVA/PVP (6/4 weight composition) was dissolved in distilled water at 95°C, and then mixed with crushed *Aloe vera* gel by a physical stirrer at room temperature to give a PVA/PVP/*Aloe vera* solution (Fig. 1). The dried content of *Aloe vera* gel was in the range of 0.4≈1.2 wt %, and the solid concentration of the total PVA/PVP/*Aloe vera* solution was 15 wt %. The solutions were then poured into petri dishes at room temperature. The solutions were maintained at room temperature for 1 h in order to remove air bubbles. Hydrogels from a mixture of *Aloe vera* and PVA/PVP were made by freeze-thawing, ^{60}Co gamma-ray irradiation, or a two-step process of freezing-thaw and ^{60}Co gamma-ray irradiation. A mixture of PVA/PVP/*Aloe vera* was exposed to gamma irradiation doses of 25, 35, and 50 kGy to evaluate the effect of irradiation on the physical properties of hydrogels. Freeze-thaw was repeated up to 3 times to crosslink the PVA/PVP/*Aloe vera* solution physically. Each cycle of freeze-thaw involved lowering the temperature to −70°C, maintaining the solution at this temperature for 1 h, and then raising the temperature to room temperature.

Gel content

The gel content of the hydrogels was measured by extraction in hot distilled water at 60°C for 48 h and vacuum drying at 60°C for 48 h until they reached a constant weight. The gel content can be defined by eq. (1), in which W_d is the dried gel weight after extraction, and W_i is the initial weight of the polymer.

$$\text{Gel (\%)} = \frac{W_d}{W_i} \times 100 \quad (1)$$

Degree of swelling

The degree of swelling can be described as the water absorptivity [eq. (2)] of the hydrogels. The gel samples

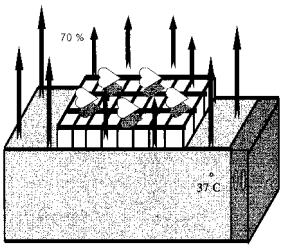

Figure 2 Apparatus for determining water loss of hydrogels.

were immersed in distilled water for 48 h at room temperature until the gel reached the equilibrium state of swelling. After the water on the surface of the swollen gels was removed with cellulose paper, the mass was determined. Dried gels were obtained by drying at 60°C until they reached a constant weight. The degree of swelling was defined by eq. (2), where W_s is the weight of the swollen gel and W_d is the weight of the dried gel.

$$\text{Water absorptivity (\%)} = \frac{W_s - W_d}{W_d} \times 100 \quad (2)$$

Gel strength

A cylindrical hydrogel specimen, with a length of 4.0 mm and a diameter of 12 mm, was used for compressive strength tests. The compressive strength tests were conducted with an Instron model 4400 universal testing machine at room temperature. A cylindrical hydrogel specimen was placed on the base, and the probe was lowered until contact was made. The probe was then lowered at 10 mm/min until 70% relative deformation, and then it was raised. The compressive strength used in this experiment is the value measured at 70% relative deformation. The mechanical properties of the hydrogels were obtained by determining the compressive strength.

Degree of water evaporation

The hydrogels were prepared by a gamma irradiation dose of 25 kGy after 2 cycles of freeze-thaw. The PVA:PVP ratio was 6:4, and the dried content of *Aloe vera* was in the range of 0.4≈1.2 wt %. The solid concentration of PVA/PVP/*Aloe vera* solution was 15 wt %. An apparatus for evaluating the water loss of hydrogels is shown in Figure 2. The hydrogels were placed on the grill of the apparatus, which was set at 37°C, and 70% relative humidity.

Wound healing test of hydrogels

Male 6-week-old Sprague-Dawley rats (200 g) were obtained from Kaeryoung Science Co. (Taejon, Korea),

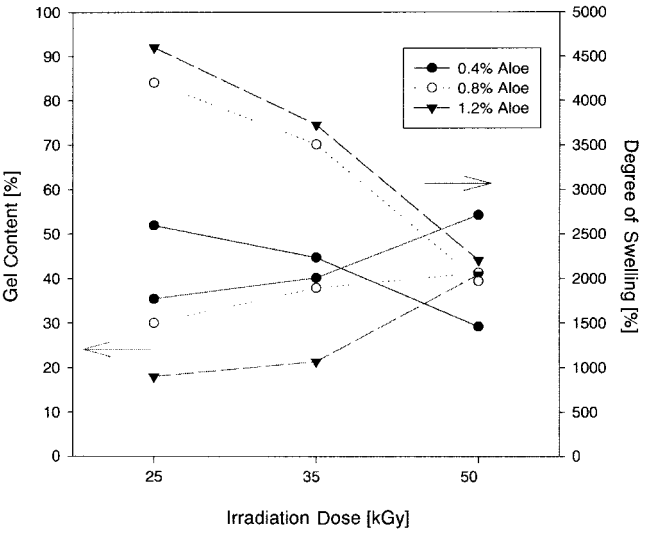

Figure 3 Gel content and degree of swelling of PVA/PVP/aloe hydrogels vs. irradiation dose.

and maintained on a standard laboratory diet. Wounds of 1 cm diameter in the skin on the backs of the rats were covered on one side with the hydrogel samples (1.5 × 1.5 × 0.3 cm), while the other side was left uncovered to check the healing effect of the synthesized hydrogels. The synthesized hydrogels in these experiments were also compared to commercial urethane membrane used to mimic human skin. PVA/PVP/*Aloe vera* hydrogels made by the two-step process of freeze-thaw and gamma-ray irradiation were used for the healing tests on rats. Both the synthesized hydrogels and the commercial urethane membrane were replaced with new ones every 3 days. Healing was evaluated as the percentage of the healed area

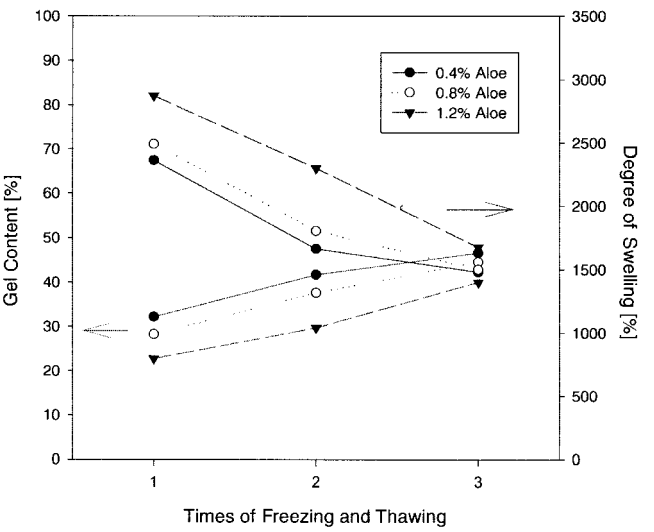

Figure 4 Gel content and degree of swelling of PVA/PVP/aloe hydrogels vs. cycles of freeze-thaw.

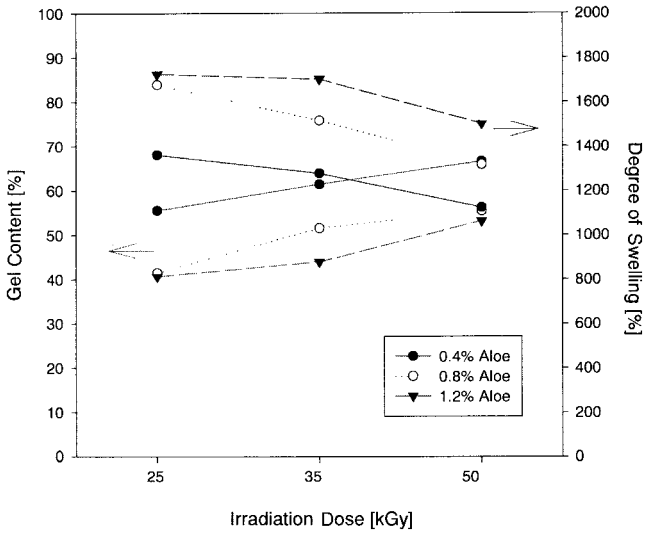

Figure 5 Gel content and degree of swelling of PVA/PVP/aloe hydrogels vs. irradiation dose after 1 cycle of freeze-thaw.

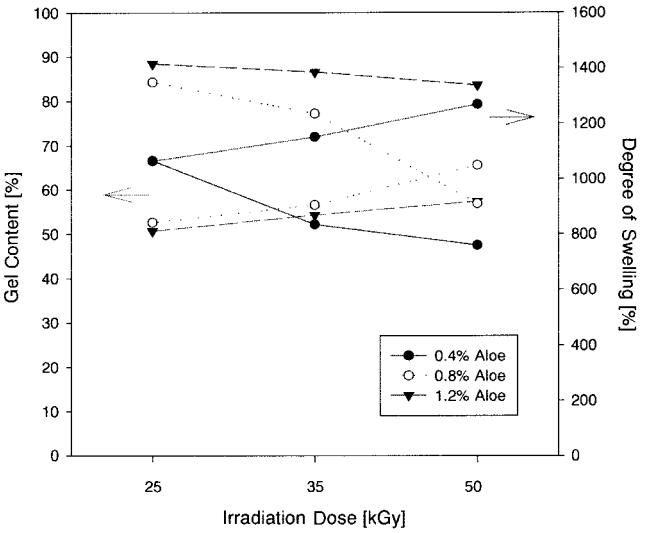

Figure 7 Gel content and degree of swelling of PVA/PVP/aloe hydrogels vs. irradiation dose after 3 cycles of freeze-thaw.

compared to the original wound area. The healing test was repeated five times for each case, and then the healing effect was evaluated. On a certain postoperative day, macroscopic observation of wound status was made. This observation was repeated daily for 21 days.

RESULTS AND DISCUSSION

Gel content and degree of swelling

Figure 3 shows the gelation behavior and the degree of swelling behavior of the hydrogels that were synthesized by gamma irradiation. Gel content was in the range of 18≈57%. Gel content increased as *Aloe vera* content in PVA/PVP/*Aloe vera* decreased, and as irradiation dose increased. The formation of the gel explains the fact that a crosslinking network is formed between PVA, PVP and *Aloe vera* by gamma rays. Gel content in this experiment was continuously decreased as the amount of *Aloe vera* in PVA/PVP/*Aloe vera* increased, because *Aloe vera* is not crosslinked by radiation. Degree of swelling was in the range 1400≈4600%. Degree of swelling increased as the concentration of *Aloe vera* in PVA/PVP/*Aloe vera* in-

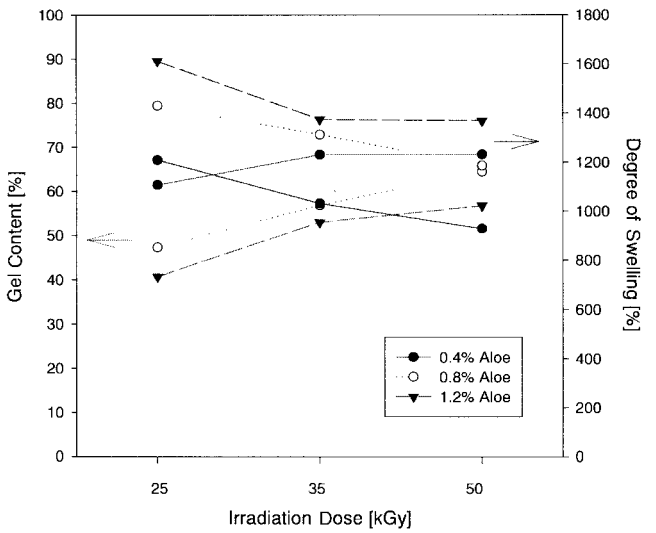

Figure 6 Gel content and degree of swelling of PVA/PVP/aloe hydrogels vs. irradiation dose after 2 cycles of freeze-thaw.

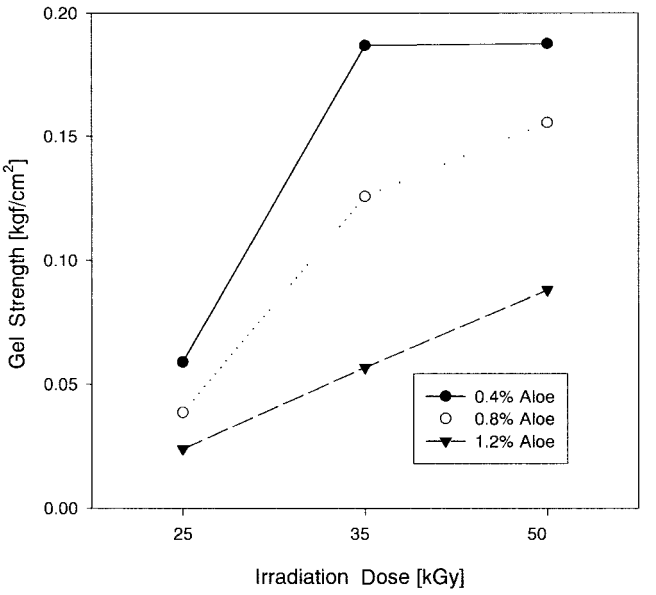

Figure 8 Gel strength of PVA/PVP/aloe hydrogels vs. irradiation dose.

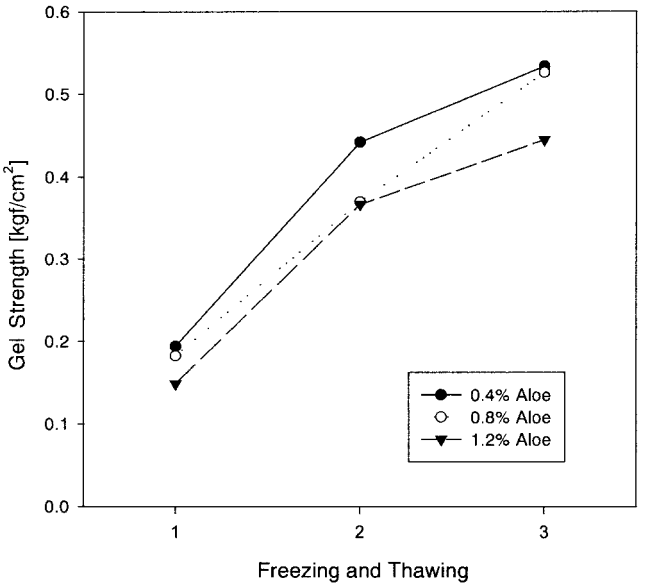

Figure 9 Gel strength of PVA/PVP/aloe hydrogels vs. cycles of freeze-thaw.

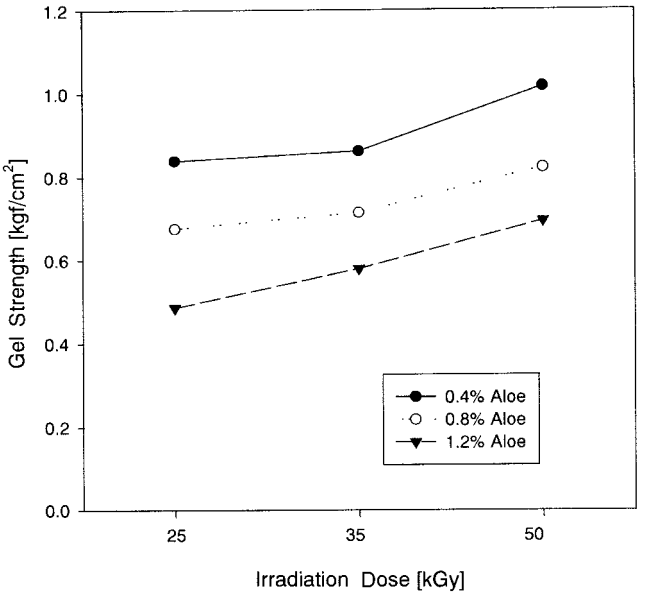

Figure 11 Gel strength of PVA/PVP/aloe hydrogels vs. irradiation dose after 2 cycles of freeze-thaw.

creased, and as irradiation dose decreased. The swelling percent was inversely proportional to the gel percent.

The gelation and swelling behavior of the hydrogels synthesized by repeated cycles of freeze-thaw are shown in Figure 4. Gel content was in the range 23≈50%. Gel content increased as the content of *Aloe vera* in PVA/PVP/*Aloe vera* decreased, and as freeze-thaw was repeated. The repeated freezing and thawing caused the gel content to increase. It is well known that, in PVA,[10] this process results in the formation of crystallites that serve as physical crosslinks to render the material insoluble in water. Gel content in this experiment was continuously decreased as the composition of *Aloe vera* in PVA/PVP/*Aloe vera* increased because *Aloe vera* is not crosslinked by freeze-thaw. The degree of swelling was in the range of 1400≈2900%. Degree of swelling increased as the content of *Aloe vera* in PVA/PVP/*Aloe vera* increased, and as the number of repeated cycles of freeze-thaw decreased.

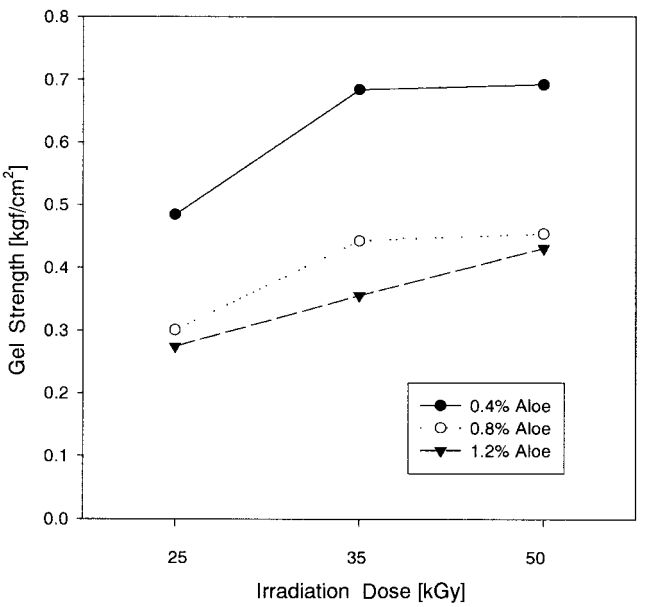

Figure 10 Gel strength of PVA/PVP/aloe hydrogels vs. irradiation dose after 1 cycle of freeze-thaw.

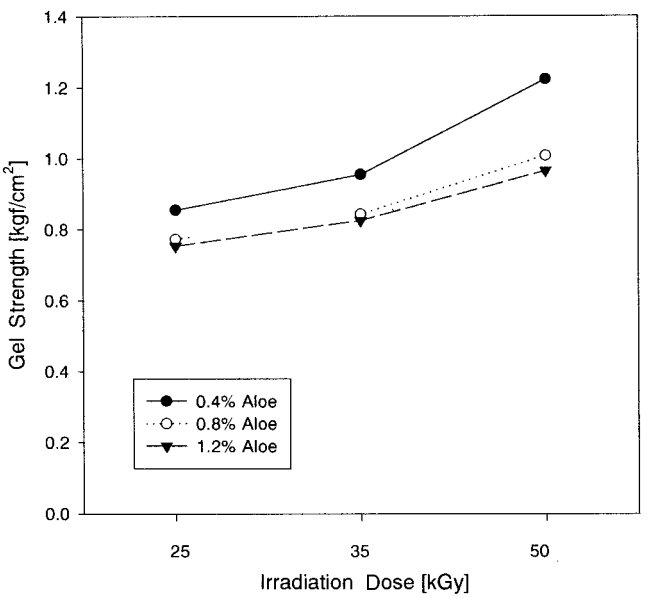

Figure 12 Gel strength of PVA/PVP/aloe hydrogels vs. irradiation dose after 3 cycles of freeze-thaw.

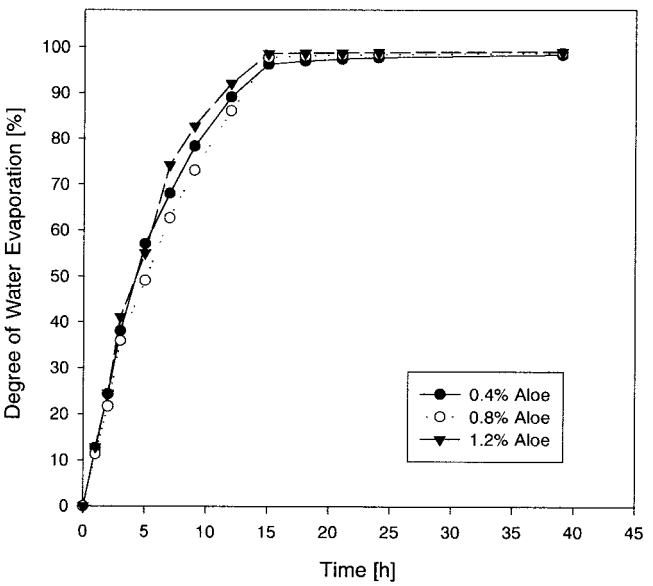

Figure 13 Degree of water evaporation of PVA/PVP/aloe hydrogels vs. time.

The gelation and degree of swelling behavior of the hydrogels synthesized by gamma irradiation after 1 cycle of freeze-thaw are shown in Figure 5. Gel content was in the range of 40≈67 %. Gel content increased as the content of *Aloe vera* in PVA/PVP/*Aloe vera* decreased, and as irradiation dose increased. Degree of swelling was in the range of 1120≈1730 %. Degree of swelling increased as the content of *Aloe vera* in PVA/PVP/*Aloe vera* increased, and as irradiation dose decreased.

The gelation and degree of swelling behavior of the hydrogels synthesized by gamma irradiation after 2 cycles of freeze-thaw are shown in Figure 6. Gel content was in the range of 40≈69%. Degree of swelling was in the range of 940≈1600%. Figure 7 shows the gelation and degree of swelling behavior of the hydrogels that were synthesized by gamma irradiation after 3 cycles of freeze-thaw. Gel content was in the range of 50≈80 %. Degree of swelling was in the range of 750≈1450%.

Crosslinking by radiation transforms a linear polymer into a three-dimensional molecule, resulting in a significant increase in molecular mass, lower solubility in organic solvents, and improved mechanical properties. Degradation results in a decrease in molecular mass, and has the opposite effect on the physical properties of the polymer. Crosslinking and degradation occur simultaneously. However, the ratio of their rates depends on the chemical structure of the polymer, its physical state, and the irradiation state. Polymers are generally divided into those that predominantly crosslink and those that predominantly degrade. PVA and PVP are easily crosslinked in their homogeneous mixture with water. A natural product such as *Aloe vera* tends to degrade on irradiation. Therefore, the addition of *Aloe vera* gel in PVA/PVP solution results in a decrease in the gelation of hydrogels.

Gel strength

The compressive strength used in this experiment is the value measured at 70% relative deformation. The gel strength of the hydrogels was obtained by determining their compressive strength. We measured the compressive strength of the hydrogels made by gamma irradiation (Fig. 8), those made by freeze-thaw (Fig. 9) and those made by two cycles of freeze-thaw and gamma irradiation (Figs. 10–12). The compressive strength increased as the concentration of *Aloe vera* in PVA/PVP/*Aloe vera* decreased, and as the irradiation dose increased. PVA/PVP/*Aloe vera* composition and irradiation dose had a great influence on the compressive strength of the hydrogels. Natural products like *Aloe vera* tend to degrade on irradiation. Therefore, the addition of *Aloe vera* gel to PVA/PVP solution results in a decrease in the compressive strength of hydrogels. It was shown that the compressive strength of each hydrogel was proportional to its degree of gelation. The compressive strength of hydrogels prepared by freeze-thaw was larger than that of the ones made by the gamma irradiation. When two cycles of freeze-thaw and gamma irradiation were used for making hydrogels, the compressive strength was greatly improved through the synergistic effect of both the physical crosslinking caused by freeze-thaw and the chemical crossslinking caused by radiation.

Degree of water evaporation

To systematically measure evaporative water loss for the synthesized hydrogels, they were placed on the

TABLE I
Characteristics of Healing Process

No Dressing	Polyurethane	Hydrogal
Formation of scar Slow healing rate (21 days for healing)	No visible wound after dressing Difficult absorption of exudates from wound Formation of scar	Good absorption of exudates from wound Good detachment of gel from wound Visible wound after dressing Fast healing rate (15 days for healing)

grill of a water bath that was kept at a temperature of 37°C and 70 % relative humidity. Evaporative water loss was measured gravimetrically for the hydrogels with various contents of *Aloe vera*. The hydrogels were prepared by an irradiation dose of 25 kGy after two cycles of freeze-thaw. The evaporative water loss values for the hydrogels are shown in Figure 13. Evaporative water loss continued to rise steadily up to 15 h and then leveled off. No significant differences were observed in the evaporation velocity among the compositions of hydrogels.

Wound healing tests

PVA/PVP/*Aloe vera* hydrogels made by two cycles of freeze-thaw and ^{60}Co gamma-ray irradiation were used for the healing tests on rats. Wounds of 1 cm diameter were formed in the skin on the backs of rats and partially covered with the hydrogel, leaving the other part uncovered. The hydrogels synthesized in these experiments were also compared with commercial urethane membrane used to mimic human skin. At a certain postoperative day, macroscopic observations of wound status were made. The wounds without dressing dried quickly and scabbed. The wound covered with commercial polyurethane membrane could not effectively absorb the exudates from wound (Table I). The PVA/PVP/*Aloe vera* hydrogels had a better curing effect than either the absence of dressing or commercial polyurethane membranes. The wounds were healed 15 days after PVA/PVP/*Aloe vera* hydrogels were applied, while wounds with no dressing healed after 21 days (Fig. 14).

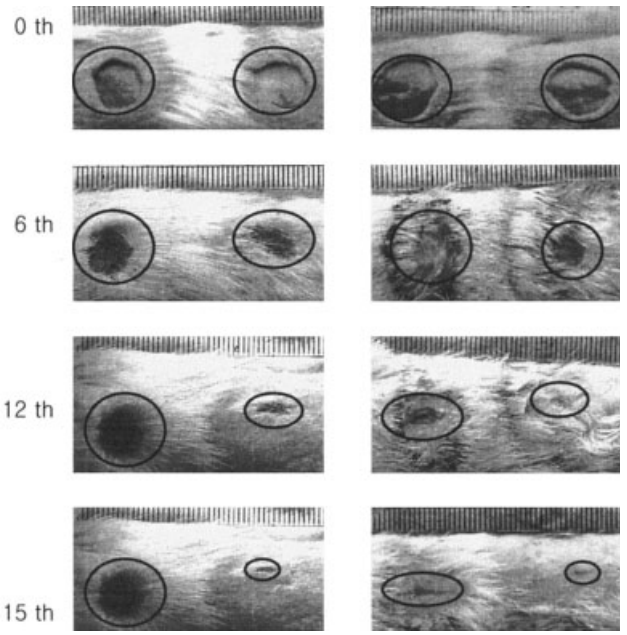

Figure 14 Healing process of wound using: (a) no dressing (left), PVA/PVP/aloe hydrogel (right), (b) Tegaderm (left), PVA/PVP/aloe hydrogel (right).

CONCLUSIONS

In this work, attempts were made to prepare hydrogels for wound dressing that consisted of PVA, PVP, and *Aloe vera*. The hydrogels were made from a mixture of *Aloe vera* and PVA/PVP by freeze-thaw, gamma-ray irradiation, or a two-step method of freeze-thaw and gamma-ray irradiation. The physical properties of the hydrogels, such as gelation and gel strength, were higher when two cycles of freeze-thaw and irradiation were used than when only irradiation was utilized. Gel content and gel strength increased as the concentration of *Aloe vera* in PVA/PVP/*Aloe vera* decreased, and as irradiation dose and repetition of freeze-thaw increased. The swelling degree of hydrogels obtained from only the irradiation process was much higher than that of those obtained from freeze-thaw or the two-step method. Swelling degree increased as the concentration of *Aloe vera* in PVA/PVP/*Aloe vera* increased, and as irradiation dose and repeated cycles of freeze-thaw decreased. The degree of water evaporation increased rapidly up to 5 h, continued to rise steadily up to 15 h and then leveled off. The PVA/PVP/*Aloe vera* hydrogel had a better curing effect than the absence of dressing and commercial urethane membranes.

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