Preparation and Characterization by Radiation of Poly(vinyl alcohol) and Poly(*N*-vinylpyrrolidone) Hydrogels Containing Aloe Vera

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ABSTRACT: In these studies, hydrogels for wound dressings were made from a mixture of aloe vera and poly(vinyl alcohol) (PVA)/poly(*N*-vinylpyrrolidone) (PVP) by freezing and thawing, γ-Ray irradiation, or a two-step process of freezing and thawing and γ-ray irradiation. We examined the physical properties, including gelation, water absorptivity, gel strength, and degree of water evaporation, to evaluate the applicability of these hydrogels for wound dressings. The PVA:PVP ratio was 6:4, the dry weight of aloe vera was in the range 0.4–1.2 wt %, and the solid concentration of the PVA/PVP/aloe vera solution was 15 wt %. We used γ radiation doses of 25, 35, and 50 kGy to expose mixtures of PVA/PVP/aloe vera to evaluate the effect of radiation dose on the physical properties of the hydrogels. Gel content and gel strength increased as the concentration of aloe vera in the PVA/PVP/aloe vera gels decreased and as radiation dose increased and the number of freeze–thaw cycles was increased. The swelling degree was inversely proportional to the gel content and gel strength. J Appl Polym Sci 90: 1477–1485, 2003

Key words: hydrogels; gels; radiation; hydrophilic polymers

INTRODUCTION

Hydrogels are most often defined as two-component systems where one of the components is a hydrophilic polymer, insoluble in water because of a three-dimensional network joining as chains, and the second one is water. These systems may swell in water until an equilibrium state is reached 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—, and —SO_3H, and 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 have electrostatic or hydrophobic interactions.

The possible use of hydrogels to replace damaged tissue was our main interest for this synthesis and detailed investigation. 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 living and nonliving tissue. Thus, they moderate the physical abnormality of the boundary. They usually show good biocompatibility when 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 dressings, enzyme immunoassays, catheters, and drug-delivery systems.[2]

Hydrogels may be classified as homopolymer hydrogels, copolymer hydrogels, multipolymer hydrogels, and 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 the swelling of a first network in a monomer and the reaction of the latter to form a second intermeshing network structure.[3] The formation of copolymer hydrogels or multipolymer hydrogels is attractive because these processes impart a variety of important chemical and physical properties for medical applications by the combination of the different monomeric units.

Natural polymers, such as chitin, chitosan, alginate, and aloe vera, have been used for dressing wounds because they play an important role in the healing process. However, natural polymers have been considered limited in their applications for wound-dress-

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ing materials because of their shortage of processing and mechanical properties. A combination of natural and synthetic polymers can endow the optimal properties necessary for wound repair.

Aloe vera is a member of the Liliaceae family. The parenchymatic tissue of aloe vera leaves contains over 98–99% water, and more than 60% of the dry matter is made up of polysaccharides.[4] The fresh leaves of aloe vera contain 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 parenchymatous tissue, which has been used for the topical treatment of skin burns and wounds.[5] Aloe vera has been used in a host of curative purposes, including the treatment of skin disorders and for healing burns and wounds. The fresh gel, juice, or formulated products have been used for medical and cosmetic purposes and for general health. Despite its wide use as 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 alcohol) (PVA) has been frequently used in the preparation of various membranes and hydrogels.[7] Poly(*N*-vinylpyrrolidone) (PVP) hydrogel has excellent transparency and biocompatibility. PVP has been used as the main component of temporary skin covers or wound dressings.[8]

Irradiation is recognized as a very suitable tool for 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, and the lack of a need to add any initiators and crosslinkers that would be possibly harmful and difficult to remove. These characteristics make irradiation the method of choice in the synthesis of hydrogels.[9]

In this work, attempts were made to prepare the hydrogels for wound dressing that consisted of PVA, PVP, and aloe vera. We examined the physical properties, including gelation, swelling, gel strength, and degree of water evaporation to evaluate the usefulness of these hydrogels for wound dressing. PVA/PVP/aloe vera hydrogels were used for healing tests on rats.

EXPERIMENTAL

Materials

PVP [weight-average molecular weight (M_w) = 1.3 $\times 10^6$] and PVA ($M_w = 8.5 \times 10^4$ to 1.46×10^5) were supplied by Aldrich Chemical Co. Fresh aloe vera (aloe vera barbadensis Miller) plant was obtained from a farm in Korea. Distilled water was used as a solvent in all of the experiments.

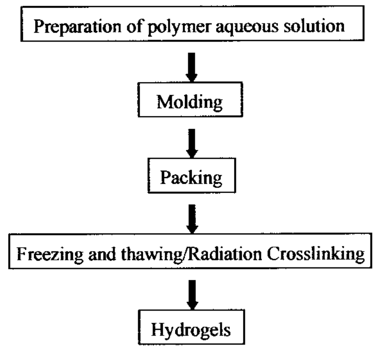

Figure 1 Flow chart for the preparation of hydrogels by radiation crosslinking.

Preparation of the hydrogels

The aloe vera leaf consists of three layers. The first is the thick cuter green rind. The second is a viscous, jelly-like mucilate layer into which vascular bundles 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, which has a 98% water content, was harvested from the green leaves, ground in a crusher, and homogenized.

PVA/PVP (6/4 w/w) was dissolved in distilled water at 95°C and was then mixed with the crushed aloe vera gel with a physical stirrer at room temperature to produce the PVA/PVP/aloe vera solution (Fig. 1). The dried content of the aloe vera gel was in the range 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 a petri dish at room temperature. The solution was kept at room temperature for 1 h to remove air bubbles. Hydrogels from a mixture of aloe vera and PVA/PVP were made by freezing and thawing, ^{60}Co γ-ray irradiation, or two freeze–thaw steps and ^{60}Co γ-ray irradiation. A mixture of PVA/PVP/aloe vera was exposed to γ-irradiation doses of 25, 35, and 50 kGy to evaluate the effect of radiation dose on the physical properties of the hydrogels. The freezing and thawing cycle was repeated up to three times to crosslink the PVA/PVP/aloe vera solution physically. In each freeze–thaw cycle, we decreased the temperature to -70°C, allowed the hydrogel to stand at this temperature for 1 h, and then raised 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 the hydrogels reached a constant weight. The gel content was defined as follows:

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

where W_d is the dried gel weight after extraction and W_i is the initial weight of the polymer.

Degree of swelling

The degree of swelling could be described as the water absorptivity of the hydrogels. The gel samples 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. The dried gels were obtained by drying at 60°C until they reached a constant weight. The degree of swelling was defined as follows:

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

where W_s is the weight of the swollen gels.

Gel strength

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

Degree of water evaporation

The hydrogels were prepared with a γ-irradiation dose of 25 kGy after freeze–thaw cycles. The PVA:PVP ratio was 6:4, the dried content of aloe vera was in the range 0.4–1.2 wt %, and the solid concentration of the PVA/PVP/aloe vera solution was 15 wt %. The apparatus used for the evaluation of the water loss of the 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 tests of the hydrogels

Rats (200 g) were anesthetized with diethyl ether and kentamine, and then, the dorsal fur was removed with electric clippers. The skin was cleansed with H_2O_2. After two wounds of 1 cm diameter in the dorsum were prepared, the skin of the rats was disinfected with povidone iodine topical solution. Wounds 1 cm in diameter were made in the skin on the backs of rats and were covered with the hydrogel samples (1.5 $\times$ 1.5 $\times$ 0.3 cm), and no covering was placed on the other side so the healing effect of the synthesized hydrogels could be checked. The synthesized hydrogels in these experiments were also compared with a commercial urethane membrane to mimic human skin. PVA/PVP/aloe vera hydrogels made by the two-step process of freezing and thawing and γ-ray irradiation were used for the healing tests on the 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 from the original wound area. The healing test was repeated five times for each case, and then, the healing effect was evaluated. At a certain postoperative day, macroscopic observation of wound status was made. This observation was repeated daily for 15 days. After all of the experiments were completed, all of the rats were killed with an overdose of kentamine.

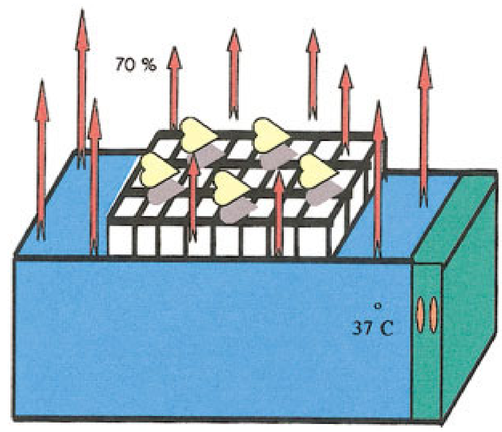

Figure 2 Apparatus for the determination of water loss in the hydrogels.

RESULTS AND DISCUSSION

Gel content and degree of swelling

Hydrogels are prepared by the swelling of crosslinked networks in water or biological fluids containing large amounts of water. In many situations, water may be present during the initial formation of the crosslinked network. There are several methods of preparing crosslinked hydrogels, including radiation and chemical crosslinking. Radiation reactions utilize electron beams, γ rays, X-rays, or ultraviolet light to excite a polymer and produce a crosslinked structure. Chemical crosslinking needs at least one difunctional, small-molecular-weight crosslinking agent. This agent usu-

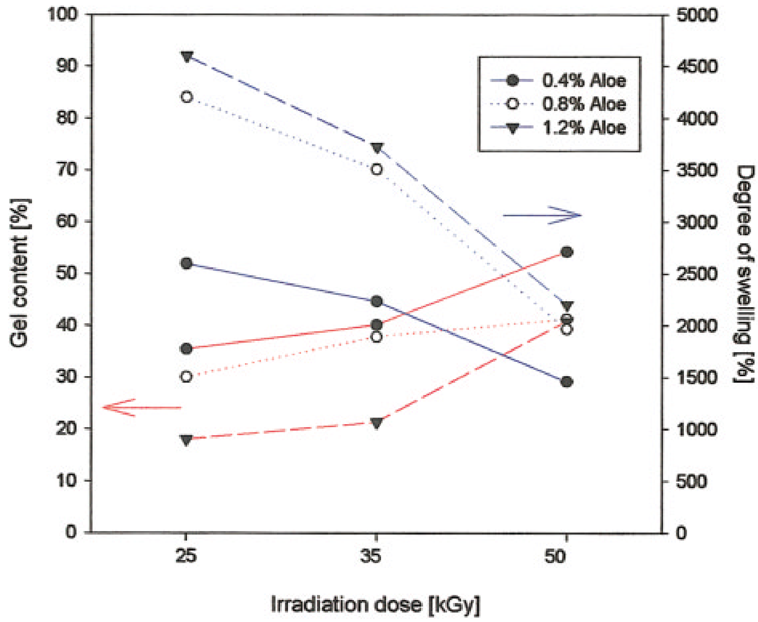

Figure 3 Gel content and degree of swelling of PVA/PVP/aloe hydrogels versus radiation dose.

ally links two longer molecular weight chains through its difunctional or multifunctional groups. Radiation crosslinking can easily be adjusted by control of the radiation dose and is reproducible. The finished product contains no residual substances required to initiate the chemical crosslinking, which can restrict the application possibilities or increase the failure rate.

Figure 3 shows the gelation behavior and degree of swelling behavior of the hydrogels that were synthesized by γ irradiation. The gel content was in the range 18–57%. The gel content increased as the aloe vera amount in PVA/PVP/aloe vera decreased and as radiation dose increased. The formation of the gel explains the fact that a crosslinking network was formed between PVA, PVP, and aloe vera by γ rays. The gel content in this experiment continuously decreased as the amount of aloe vera in PVA/PVP/aloe vera increased because aloe vera was not crosslinked by radiation. The degree of swelling was in the range 1400–4600%. The degree of swelling increased as concentration of aloe vera in PVA/PVP/aloe vera increased and as the radiation dose decreased. The swelling percentage was inversely proportional to the gel percentage.

The gelation and swelling behaviors of the hydrogels, which were synthesized by repeated freezing and thawing, are shown in Figure 4. The 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 freezing and thawing was repeated. The repeated freezing and thawing caused the gel content to increase. It is well known that this PVA procedure[10] results in the formation of crystallites that serve as physical crosslinks and render the material insoluble in water. The gel content in this experiment continuously decreased as the composition of aloe vera in PVA/PVP/aloe vera increased because aloe vera was not crosslinked by the freezing and thawing procedure. The degree of swelling was in the range 1400–2900%. The degree of swelling increased as the content of aloe vera in PVA/PVP/aloe vera increased and as the repeated cycles of freezing and thawing were decreased.

The gelation and degree of swelling behavior of the hydrogels that were synthesized by γ irradiation after one freeze–thaw cycle are shown in Figure 5. The gel content was in the range 40–67%. The gel content increased as the content of aloe vera in PVA/PVP/aloe vera decreased and as the radiation dose increased. The degree of swelling was in the range 1120–1730%. The degree of swelling increased as the content of aloe vera in PVA/PVP/aloe vera increased and as the radiation dose decreased.

The gelation and degree of swelling behavior of the hydrogels that were synthesized by γ irradiation after two freeze–thaw cycles are shown in Figure 6. The gel content was in the range 40–69%. The degree of swelling was in the range 940–1600%. Figure 7 shows the gelation and degree of swelling behavior of the hydrogels that were synthesized by γ irradiation after three freeze–thaw cycles. The gel content was in the range 50–80%. The degree of swelling was in the range 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 phys-

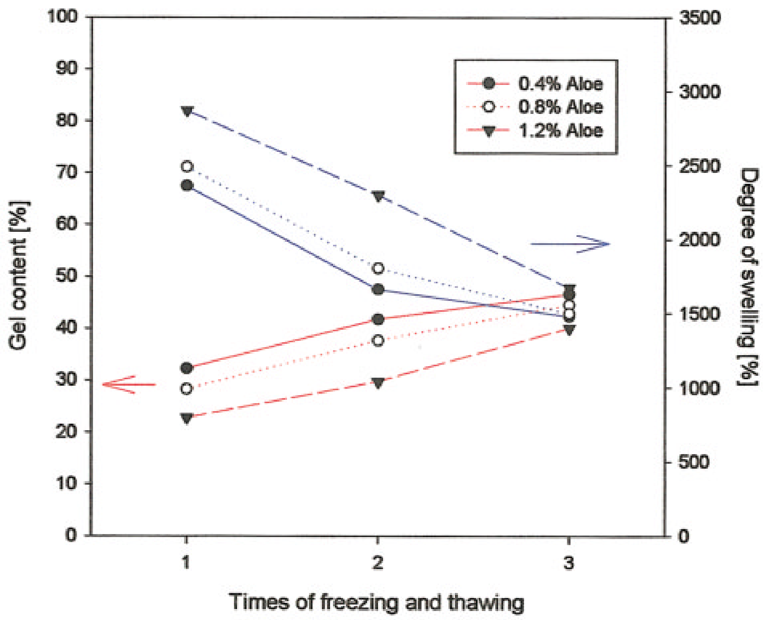

Figure 4 Gel content and degree of swelling of PVA/PVP/aloe hydrogels versus freezing and thawing.

ical 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 homogeneous mixtures with water. Natural products, such as aloe vera, tend to degrade on irradiation. Therefore, the addition of aloe vera gel in PVA/PVP solution resulted in a decrease in the gelation of the hydrogels.

Gel strength

The compressive strength used in this experiment was the value measured at 70% relative deformation. The gel strength of the hydrogels was obtained by the determination of their compressive strength. We measured the compressive strength for the hydrogels that

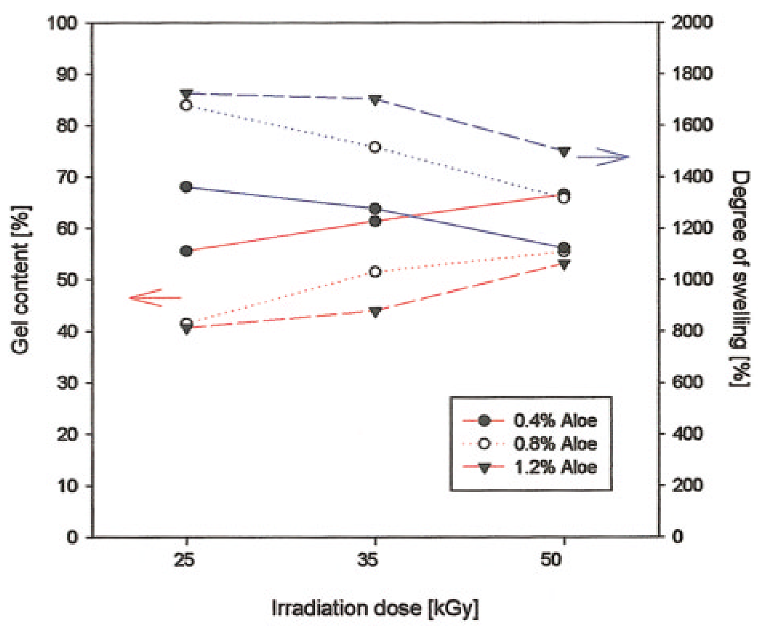

Figure 5 Gel content and degree of swelling of PVA/PVP/aloe hydrogels versus radiation dose after one freeze–thaw cycle.

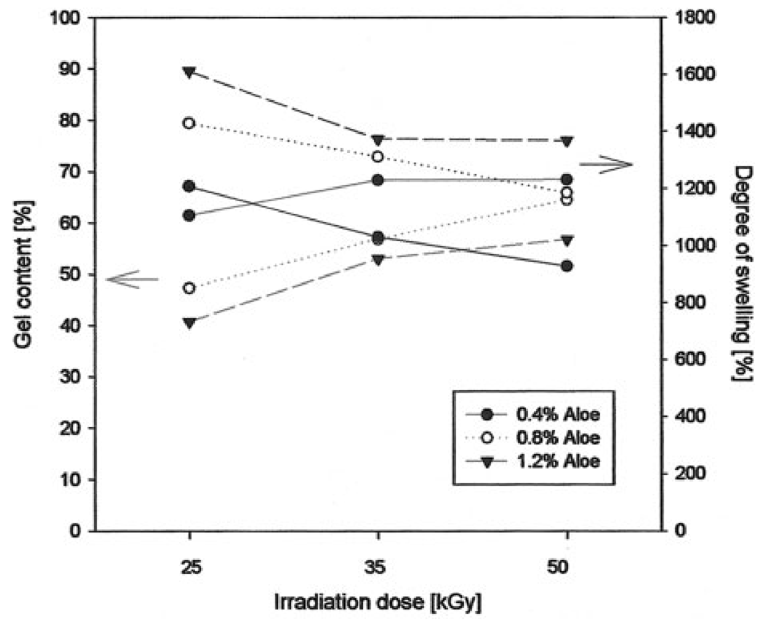

Figure 6 Gel content and degree of swelling of PVA/PVP/aloe hydrogels versus radiation dose after two freeze–thaw cycles.

were made by γ irradiation (Fig. 8), freezing and thawing (Fig. 9), and two steps of freezing and thawing and γ irradiation (Figs. 10–12). The compressive strength increased as the concentration of aloe vera in PVA/PVP/aloe vera decreased and as the radiation dose increased. The PVA/PVP/aloe vera composition and radiation dose had a great influence on the compressive strength of the hydrogels. Natural products, such as aloe vera, tend to degrade on irradiation. Therefore, the addition of aloe vera gel in the PVA/PVP solution resulted in a decrease in the compressive strength of the hydrogels. It was shown that the compressive strength of the hydrogel was proportional to the degree of gelation. The compressive strength of the hydrogel prepared by freezing and thawing was larger than the γ irradiation. When two steps of freezing and thawing and γ irradiation were used to make the hydrogels, the compressive strength of the hydrogel

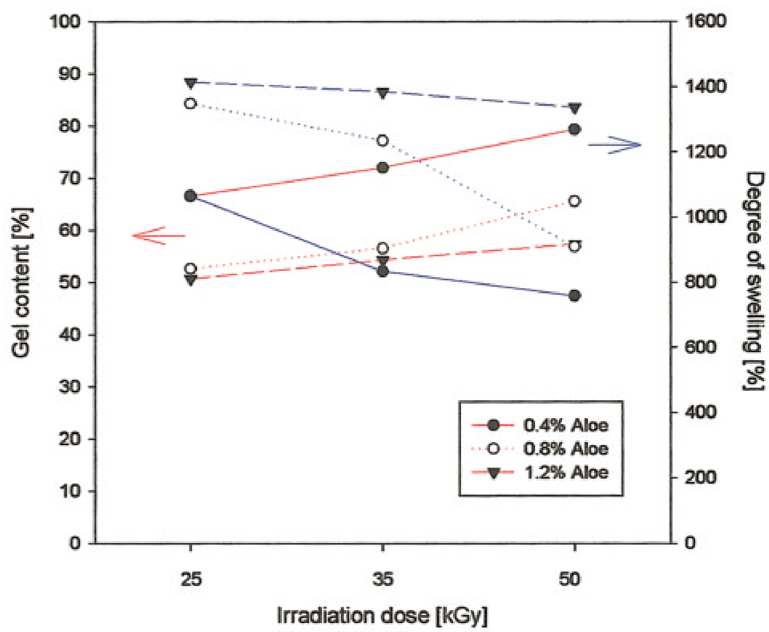

Figure 7 Gel content and degree of swelling of PVA/PVP/aloe hydrogels versus radiation dose after three freeze–thaw cycles.

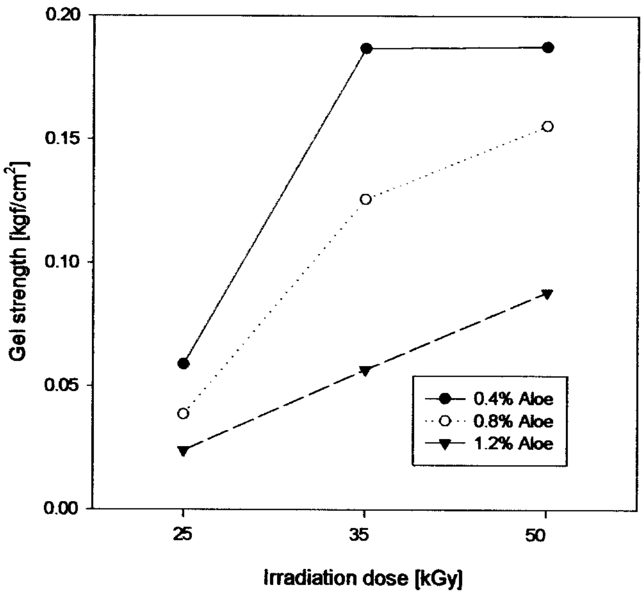

Figure 8 Gel strength of PVA/PVP/aloe hydrogels versus radiation dose.

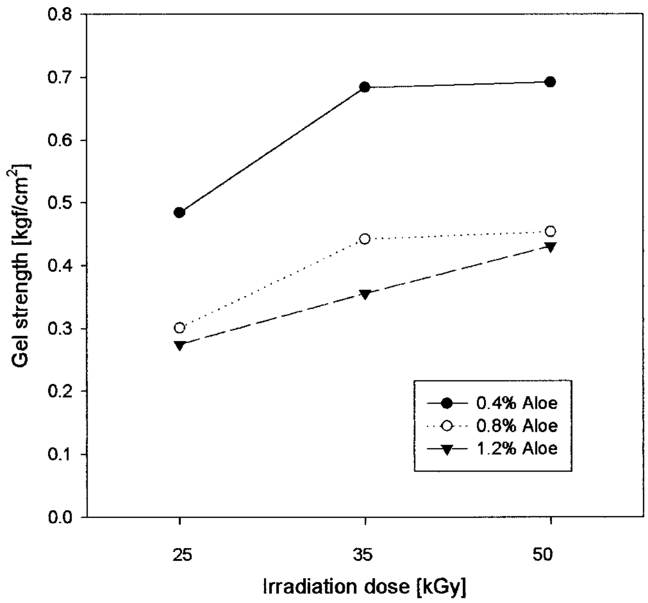

Figure 10 Gel strength of PVA/PVP/aloe hydrogels versus radiation dose after one freeze–thaw cycle.

was greatly improved through the synergistic effect of both the physical crosslinking of freezing and thawing and the chemical crosslinking of radiation.

Degree of water evaporation

To systematically measure evaporative water loss for the synthesized hydrogels, we placed them on the grill of a water bath, which was kept at 37°C and 70% relative humidity. Evaporative water loss was measured gravimetrically for the hydrogels, which involved various contents of aloe vera. The hydrogels were prepared with a radiation dose of 25 kGy after two freeze–thaw cycles. The evaporative water losses 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 between the compositions of hydrogels.

Wound-healing tests of the hydrogels

Aloe vera has been used therapeutically for a long time. It is a familiar ingredient in a range of widely

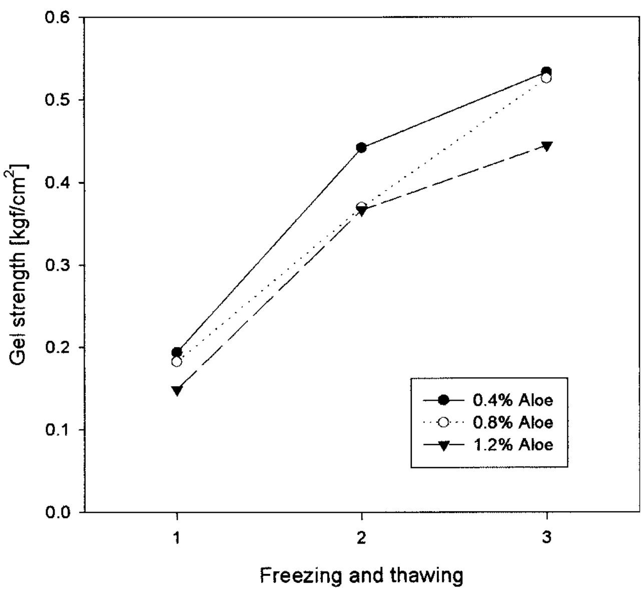

Figure 9 Gel strength of PVA/PVP/aloe hydrogels versus freezing and thawing.

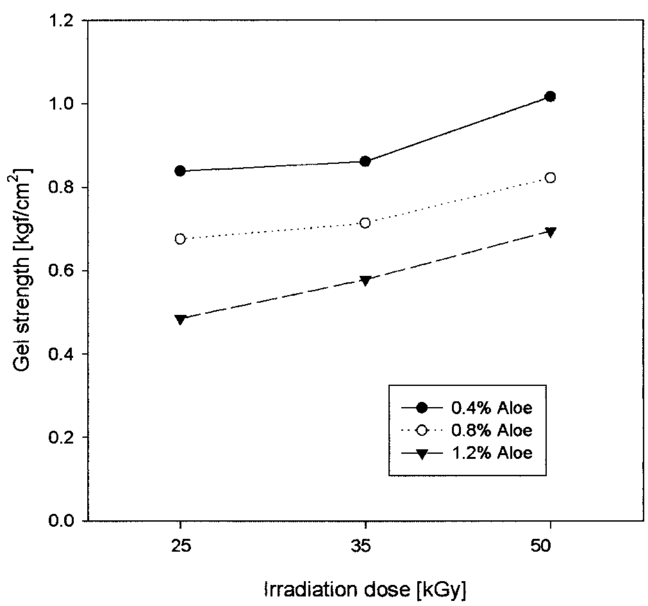

Figure 11 Gel strength of PVA/PVP/aloe hydrogels versus radiation dose after two freeze–thaw cycles.

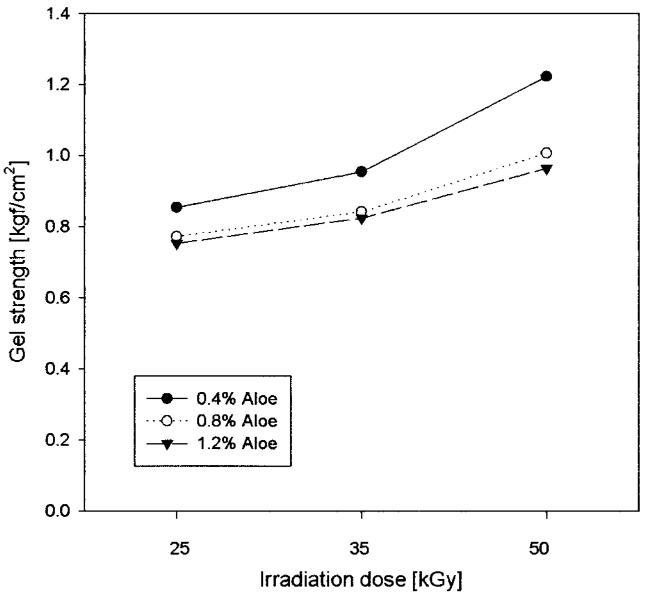

Figure 12 Gel strength of PVA/PVP/aloe hydrogels versus radiation dose after three freeze–thaw cycles.

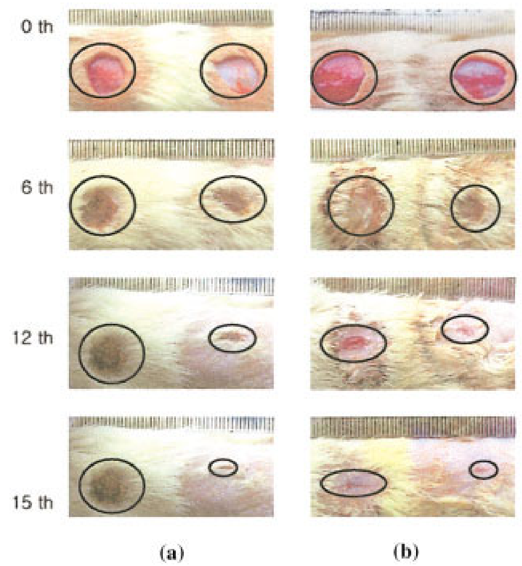

Figure 14 Healing process of wound with (a) no dressing (left) and PVA/PVP/aloe hydrogel (right) and (b) Tegaderm (left) and the PVA/PVP/aloe hydrogel (right).

available healthcare and cosmetic products. There is now less said about doubts as to the efficacy of the material, although there are some allergic side effects.[11]

A wound to the skin may pierce two layers, the epidermis and dermis, and it may also damage the appendages. The epidermis is repaired in three phases, the migration of cells, proliferation, and maturation, whereas new connective tissue is found in the dermis.[12]

Aloe vera gel is known to possess an anesthetic effect, bactericidal action, and an antithromboxane effect. The recognition of the possible multifarious activities of aloe vera gel on heat burn, electrical burns, and frostbite in guinea pigs and rabbits and in clinical studies with humans has demonstrated a therapeutic potential across the wide variety of soft-tissue injuries. Aloe vera gel is known to penetrate tissue, relieve pain, reduce inflammation, and increase blood supply by inhibiting the synthesis of thromboxane A_2, a potent vasoconstrictor.[13]

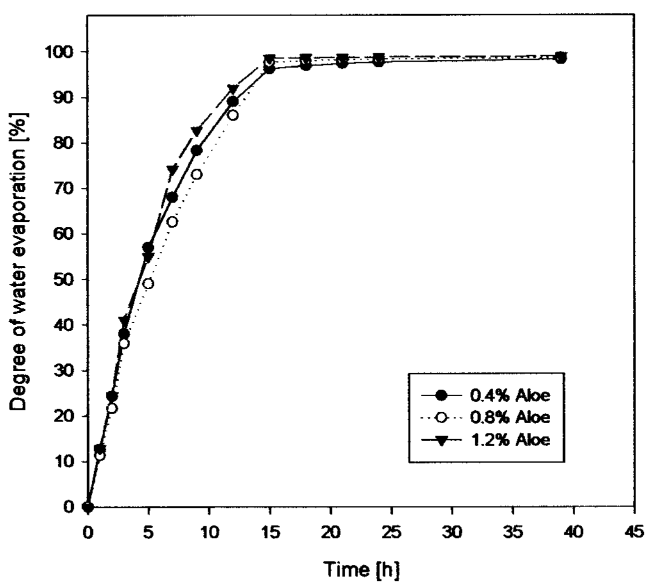

Figure 13 Degree of water evaporation of PVA/PVP/aloe hydrogels versus time.

PVA/PVP/aloe vera hydrogels made by two freeze–thaw cycles and ^{60}Co γ-ray irradiation were used for healing tests in rats. A wound 1 cm in diameter was made in the skin on the back of rat and was covered with the hydrogel, with no covering on the other side. The synthesized hydrogels in these experiments were also compared with a commercial urethane membrane to mimic human skin. On a certain postoperative day, a macroscopic observation of the wound status was made. The wound with nondressing dried quickly and scabbed. The wound covered with the commercial urethane membrane did not dry as much as the wound with the nondressing and did not scab. However, the PVA/PVP/aloe vera hydrogel had a better curing effect than the nondressing and commercial urethane membrane. Observation continued for 15 days.

CONCLUSIONS

In this work, we prepared 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 freezing and thawing, γ-ray irradiation, or a two-step method of freezing and thawing and γ-ray irradiation. The physical properties of the hydrogels, including gelation and gel strength, were higher when two steps of freezing and thawing and irradiation were used than when only irradiation was used. The gel content and gel strength increased as the concentration of aloe vera in PVA/PVP/aloe vera decreased and as radiation dose and repetition of freezing and thawing increased. The swelling degree of hydrogels obtained from the irradiation-only process was much higher than those obtained from freezing and thawing or the two-step method of freezing and thawing and irradiation. The swelling degree increased as the concentration of aloe vera in PVA/PVP/aloe vera increased and as the radiation dose and repeated cycles of freezing and thawing 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 no dressing and the commercial urethane membrane.

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