Radiation synthesis of poly(*N*-vinyl-2-pyrrolidone)- κ -carrageenan hydrogels and their use in wound dressing applications. I. Preliminary laboratory tests

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Abstract: Poly(*N*-vinyl-2-pyrrolidone)- κ -carrageenan hydrogels (PVP-KC) were prepared by irradiating the mixtures of aqueous solutions of PVP, KC, potassium chloride, and poly(ethylene glycol) by γ -rays at different doses. Their preliminary laboratory tests were evaluated to identify their usability in wound dressing applications. For investigation of the effect of components on the gelation of PVP, sol–gel analyses were made and gel fractions of the hydrogels were determined. Mechanical experiments were conducted for both unirradiated and irradiated samples. For investigation

of the fluid uptake capacity of the hydrogels, swelling experiments were performed in pseudo-extracellular fluid solution at various temperatures. Acidity/alkalinity (pH) and electrical conductivity tests were achieved from aqueous extracts of hydrogels, and bioadhesion strength of the hydrogels was investigated on human skin. © 2005 Wiley Periodicals, Inc. *J Biomed Mater Res* 74A: 187–196, 2005

Key words: poly(*N*-vinyl-2-pyrrolidone)- κ -carrageenan hydrogels (PVP-KC); γ -rays; wound dressing applications

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INTRODUCTION

Recently, hydrogels have found a wide range of biomedical applications including controlled drug delivery systems as well as transdermal systems, replacement blood vessels, wound dressing, dental materials, ophthalmic applications, contact lenses, and a variety of other related and potential uses. Hydrogels closely resemble living tissues in their physical properties because of their relatively high water content and soft and rubbery consistency. The biocompatibility to tissue and blood coupled with water content is similar to tissue.

Poly(*N*-vinyl-2-pyrrolidone) (PVP)-based hydrogels, produced by radiation-induced crosslinking and simultaneous sterilization, have been applied successfully as local dressings on wound treatments, such as burns, skin ulcerations, and postoperative dressings. The production process of these hydrogels by using radiation processing was developed by Rosiak et al.¹

A hydrogel dressing prevents the wound from microbial contamination, inhibits the loss of body fluids, provides free flow of oxygen to the wound, and generally accelerates the healing process.

Ionizing radiation has long been recognized as a suitable tool for the formation of hydrogels. Easy process control, possibility of joining hydrogel formation and sterilization in one technological step, no necessity to add any initiators, crosslinkers, etc., having no waste, and relatively low running costs, are advantages of ionizing radiation. These advantages make irradiation a method of choice in the synthesis of hydrogels, especially for biomedical use. Radiation production of hydrogel wound dressings (HWDs) started first in Poland at the Technical University of Lodz in 1992. PVP-based dressings, obtained by e-beam irradiation, were commercialized under the registered trademarks KIK-gel® and AQUA-gel®. Since the beginning of 2003, there has been fully automatic HWD production at Instituto de Pesquisas Energeticas e Nucleares (IPEN), Brazil. The dressings, named commercially as Biogel®, were based on PVP and produced by γ -irradiation. In Japan, Takasaki Radiation Chemistry Research Establishment (JAERI) researchers have developed poly(vinyl alcohol) (PVA)-based HWDs crosslinked by e-beams. The National Center for Radiation Research and Technology (NCRRT) Egypt developed the technology of radiation synthesis

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of HWD in industrial scale. Recently, research has been performed at the Bhabha Atomic Research Center (BARC) India for large-scale production of HWDs based on crosslinking of PVA.²

Hydrogels of natural polymers, especially polysaccharides, have been used recently as biomaterial, because of their unique advantages such as nontoxicity, biocompatibility, biodegradability, and abundance.^{3,4}

Polysaccharides, as natural biomolecules, are obvious choices for investigation as potential wound management aids. Alginic acid/alginate, hyaluronic acid/hyaluronate, cellulose, dextran, chitin and chitosan, carrageenan, and heparin are used in wound management aids as dressing materials.⁵

Carrageenan is the generic name for the family of natural water-soluble sulfated polysaccharide with an alternating backbone consisting of $\alpha(1-4)$ -3,6-anhydro-D-galactose and $\beta(1-3)$ -D-galactose. The carrageenan fractions differ according to the number and position of the sulfate groups and to the possible presence of a 3-6 anhydrogalactose bridge. Theoretically speaking, there are three main ideal carrageenan types: κ , ι , and λ . κ -Carrageenan (KC) has one sulfate for every two sugar units with a 25% sulfate content approximated. ι -Carrageenan contains additionally a sulfo group in the 2-position of the anhydrogalactose residue. λ -Carrageenan is the most sulfated type among this group of polysaccharides. During cooling, KC, a gelling agent, forms hard and brittle gels. ι -Carrageenan is also considered a gelling agent, but it forms soft and elastic gels. λ -Carrageenan is a non-gelling galactan.

Blends of synthetic and natural polymers represent a new class of materials with better mechanical properties and biocompatibility than those of the single components. Therefore, the most recent research has focused on synthetic/natural polymer blend materials such as cellulose diacetate/PVP,⁶ starch/PVA,⁷ KC/poly(diallyl dimethyl ammonium chloride),⁸ chitosan/PVP, chitosan/PVA, chitosan/poly(ethylene oxide),⁹ alginate/poly(*N*-isopropyl acrylamide),¹⁰ and agar/PVP/poly(ethylene glycol) (PEG).¹¹ These hydrogels exhibit properties that are different from original polymers. An improved equilibrium swelling and changes in responses to pH, ionic strength, and temperature have been noted. PVP hydrogel itself is of limited applicability because of its inferior mechanical properties. So, blending PVP with other polymers has a significant role in a series of PVP hydrogels as biomedical materials. Cellulosediacetate⁶ and chitosan⁹ form miscible blends with PVP. Recently, Relleve et al.¹² prepared and characterized a series of hydrogels that were prepared by γ -irradiation of PVP and KC. They proposed that γ -irradiation of VP-KC blends results in simultaneous crosslinking of VP, grafting of VP onto KC, degradation of carrageenan into smaller chains occurring simultaneously, and eventually leads

to the formation of a hydrogel. From this complicated system, a combination of two kinds of network structures may result: an interpenetrating network (IPN), wherein carrageenan chains are trapped/entangled within the PVP network, and a grafted network, wherein the PVP network is grafted on the carrageenan backbone.

In this study, radiation synthesis of PVP-based wound dressings by using PVP, natural polymer, KC, KCl, and low-molecular-weight PEG as adhesive has been investigated. Preliminary laboratory tests of the hydrogels were conducted for the identification of their usability in wound dressing applications.

EXPERIMENTAL

Materials

PVP [molecular weight (MW) = 1,300,000; lot no.: 04917-126], and KC (lot no.:17327II) were obtained from Aldrich. PEG was obtained from Merck (MW = 600). Potassium chloride was analytical grade from Merck. Milli-Q high-performance liquid chromatography-grade water was used in the preparation of all mixtures.

The amount of ι -carrageenan impurity was determined by using the proton nuclear magnetic resonance and Fourier transform infrared (FTIR) spectra of KC. It was found that the commercial κ batch used in this work was contaminated by 16% ι .¹³

Preparation of hydrogels

Various combinations of mixtures with concentrations of PVP (3, 5, 10% w/w), KC (1, 2, 3% w/w), KCl (0.1, 0.3, 0.5% w/w), and PEG (1.5% w/w) solutions were prepared in 10 mL of deionized water at 70–80°C for 4 h, and samples were stirred occasionally by vortex, then the hot mixtures were filled in poly(ethylene terephthalate) molds (thickness of mold was approximately 3 mm), sealed, and finally irradiated at room temperature by ⁶⁰Co γ -source at the doses of 15, 25, and 35 kGy.

Characterization of hydrogels

Sol–gel analyses of hydrogels

Hydrogel samples were cut into pieces with a diameter of 3–4 mm, dried in a vacuum oven at room temperature to constant weight, and subjected to

Soxhlet extraction with deionized water as solvent. Uncrosslinked polymer was removed with this extraction from the gel structure. Extracted gels were dried again in a vacuum oven at room temperature to constant weight. The gel fraction was calculated by using initial weight of dry gel and weight of extracted dry gel.

FTIR spectrometric analysis

FTIR spectra were recorded using a Nicolet 520 model FTIR spectrophotometer in the range of 4000 and 400 cm^{-1} . To prepare the samples for FTIR measurements, solvents of each solution were evaporated and dried in a vacuum oven, and then mixed with KBr. The percentage of polymer in KBr pellets was 10 (by weight).

Swelling behavior of hydrogels in pseudo-extracellular fluid (PECF) solution

For the investigation of the swelling properties of hydrogels, PECF solution was used. The liquid formulation of PECF solution, simulated wound fluid, consists of 0.68 g of NaCl, 0.22 g of KCl, 2.5 g of NaHCO_3 , and 0.35 g of NaH_2PO_4 in 100 mL of deionized water.¹⁴ The ionic strength and pH of PECF solution were 0.48M and 7.4 ± 0.2 , respectively. Fresh hydrogels were left to swell in PECF solution at 25°C to investigate their swelling behaviors. Gels were accurately weighed and then soaked in PECF solution at room temperature. At a given time, they were removed from solvent carefully and wiped by filter papers, weighed, and placed in PECF solution. This procedure was repeated several times until a constant weight was reached for each sample. The percentage swellings of hydrogels was calculated from the difference between the initial and the final weight of the sample divided by the initial weight of the sample.

Investigation of aqueous extracts of hydrogels

For preparation of an aqueous extract from a hydrogel, 10 g of hydrogel was placed in a conical flask, and 50 mL of deionized water was added. The mixture was kept in a thermostat bath at 37°C for 72 h. After incubation, possible losses of water were filled up with water, which was used to prepare an aqueous extract.

Determinations of the pH and the conductivity of the aqueous extracts were performed at room temperature by using a Hanna pH 211 microprocessor model

pH meter and 522 model Crison conductivity meter, respectively.

Mechanical properties and adhesion tests of hydrogels

The mechanical properties were determined at room temperature by uniaxial compression experiments at a crosshead speed of 5 mm/s until failure, using a Zwick Z010 model Universal Testing Instrument and uniaxial compression module, equipped with a 1 kN compression load cell. This apparatus consists of two stainless-steel flat discs, one of which is fixed whereas the other can be moved vertically. Diameter and height of each gel were measured with a compass before the test. The average value from five measurements was retained. The mechanical properties of the hydrogels were measured in their relaxed state (after preparation).

Bioadhesion strength of the hydrogels was measured to evaluate their adhesion capability onto human skin. After applying a load of 0.1 N on the skin for 5 min, the adhesion strength of the hydrogel was measured with the Zwick Z010 model Universal Testing Instrument in ambient conditions. The measurement was performed five times for each sample to calculate the average bonding strength.

RESULTS AND DISCUSSION

Preparation of hydrogels

Polysaccharides such as agar,¹¹ KC,¹⁵ chitosan,¹⁶ and gelatin¹⁷ are generally used in the preparation of PVP hydrogels to improve the mechanical stability of PVP solution and decrease the fluidity of PVP before irradiation.

PVP/KC mixtures were prepared in the presence of KCl at various compositions for the determination of optimum KC and PVP concentration.

KC is a polyanion, and therefore salts affect its gelation behavior. To investigate the effects of K^+ ions on the physical gelation of KC, various amounts of KCl were added to 0.7% w/w KC solution. The original KC contains different alkali metal counterions. The ion concentrations of KC used in this study are as follows: K^+ , 11.3%; Ca^{2+} , 2.2%; Na^+ , 1.0% [Aldrich Data Sheet lot (17327ji) results]. Thus, it was calculated that 0.7% w/w KC consists of 0.08% w/w K^+ . However, this KC concentration (0.7% w/w) or K^+ concentration were not enough for the wall-to-wall gelation of KC.¹⁸ Upon addition of only a minute amount of KCl (0.015% w/w) to 0.7% w/w KC solution, wall-to-

wall gelation was observed. However, at the KCl concentrations $<0.015\%$ w/w, KC solution was transparent and fluid. These results indicate that the physical gelation behavior of KC is very sensitive to the amount of K^+ in the gelation medium.

PEG 1.5% w/w was also added to the ternary mixture of PVP/KC/KCl. PEG is an additive that is typically used in the case of PVP hydrogels for biomedical applications, because of its nontoxic property. It also allows changes in the rheological characteristics of hydrogels of PVP. The presence of PEG usually increases the elasticity, adhesion, and tacky properties of the hydrogels because of its plasticizing effect. The PEG chains settle among the PVP chains, avoiding crosslinking, and decrease the physical interactions between PVP chains. Moreover, Hilmy et al.¹⁹ used PEG in PVP hydrogels and they observed that the presence of PEG could improve the hydrogel barrier against bacteria.

After preparation of PVP/KC/KCl/PEG mixtures, in order to form mechanically stable and homogenous mixtures at room temperature, optimum compositions of PVP, KC, and KCl were determined. Mixtures containing 1% w/w KC and 3–5% w/w PVP were very soft and mechanically unstable. Gels containing 3% w/w KC were very stable but not homogeneous because of the bubbles formed during the preparation of mixtures. Gels containing 2% w/w KC and 10% w/w PVP were mechanically stable and homogeneous. Thus, from this step on, only the mixtures containing 2% w/w KC and 10% w/w PVP and 1.5% w/w PEG and various amounts of KCl were loaded to poly(ethylene terephthalate) molds and they were sealed, following the process of irradiation with γ -rays for the preparation of PVP-based wound dressings. γ -Radiation doses of 15, 25, and 35 kGy were exposed to evaluate the effect of irradiation dose on the properties of dressings. Twenty-five kilograys is the sterilization dose in biomedical applications and is also the preferred dose by many researchers for the preparation of wound dressings.²⁰

Sol-gel analyses of hydrogels

Figure 1 indicates that the gel fraction changes depend on the concentrations of PVP and KC. Higher gel fraction is achieved in pure PVP and the gel fraction increased with increasing PVP content and it never seemed to reach 100% of gel even in the pure PVP system. A decrease in gel fraction was observed with increasing KC concentration. Radicals, generated by the ionization of water with γ -radiation, are mostly responsible for the crosslinking of PVP. KC acts as a crosslinking inhibitor suppressing the action of the hydroxyl radical whereby the PVP competes with KC

Figure 1. Variation of gel fraction of PVP/KC hydrogels as a function of KC and PVP content in the initial mixture. Weight percentage of PVP in mixtures is 3 (■), 5 (○), and 10 (▲).

for the free radicals. Consequently, irradiation of PVP/water in the presence of KC decreases the crosslinking density of the PVP network. The effects of KCl on the gel fraction of mixtures containing 5% w/w PVP and 1–3% w/w KC and those containing 10% w/w PVP and 1–3% w/w KC are given in Figure 2(a) and (b), respectively. Increasing the concentration of KCl decreases the gel fraction. This is probably attributable to the dilution of PVP by KCl, which results in decrease in radicalic interactions in PVP macromolecules. Comparison of Figure 2(b) to Figure 3 reveals that the addition of PEG generally causes a decrease in gel fraction. This can be explained as a decrease in radicalic interactions of PVP macromolecules; or PEG, alternatively, acts as a chain transfer agent in the crosslinking of PVP.²¹ The effect of PEG on the gel fraction of PVP/KC/KCl mixtures is very dominant over the systems containing 0.5% w/w KCl and 1–3% w/w KC.

Characterization of hydrogels

FTIR analyses

FTIR spectra of pure PVP, pure KC, and PVP/KC blend are shown in Figure 4. Spectra are given in the range $2000\text{--}400\text{ cm}^{-1}$, because main chemical changes occurred in this range. Peak assignments of the KC and PVP are summarized in Table I. In the FTIR spectrum of PVP/KC hydrogel, the bands that belong to both components can be seen. These results indicate that PVP is miscible with KC.

The pyrrolidone rings in PVP contain a proton-

Figure 2. Variation of gel fraction of PVP/KC/KCl hydrogels as a function of KC and KCl content in the initial mixture. Weight percentage of PVP is 5 (a) and 10 (b). Weight percentage KCl in mixtures is 0 (■), 0.1 (○), 0.3 (▲), and 0.5 (▽). Total irradiation dose is 25 kGy.

accepting carbonyl moiety, whereas KC presents hydroxyl as a hydrogen donor. Therefore, hydrogen-bonding interactions may take place between these two chemical moieties in a blend of KC and PVP. FTIR spectra of pure PVP, pure KC, and PVP/KC blends are given in Figure 5(i) in the range of $3750\text{--}2500\text{ cm}^{-1}$ for the investigation of the hydroxyl (—OH) vibration frequency. Significant shifts from 3495 to 3401 cm^{-1} and broadening of peaks can be observed with increasing content of KC. For instance, when pure KC is compared with PVP/KC, the hydroxyl peak of the blend shifted to higher frequencies and broadened remarkably. Carbonyl groups (C=O) in the FTIR spectra of PVP and KC in blends, in the range of $2000\text{--}1500\text{ cm}^{-1}$, are shown in Figure 5(ii). The vibration frequency of carbonyl groups shifted from 1670 to 1660 cm^{-1} with increasing content of KC and/or decreasing content of PVP. These features can be attributed to the shift of the electron density that lowers the vibration transition energies associated with hydroxyl

Figure 3. Variation of gel fraction of PVP/KC/KCl/PEG hydrogels as a function of KC and KCl percentage in the initial mixture. PVP and PEG percentage in all mixtures are 10 and 1.5, respectively. Weight percentage of KCl in mixtures is 0 (■), 0.1 (○), 0.3 (▲), and 0.5 (▽). Total irradiation dose is 25 kGy.

groups of KC and carbonyl groups of PVP due to the hydrogen bond formations.²²

Chitosan, as a natural polymer, similar to carrageenans, gives miscible blends with PVP, poly(ethylene oxide), and PVA, because of hydrogen bonding.⁹ In a similar study performed by Jinghua et al.,⁶ FTIR was used to investigate the nature of cellulosediacetate–PVP interaction. Hydrogen bond formation and similar shifts were also observed in these polymers by Jinghua et al.

After clarifying the blending of PVP and KC, the effect of γ -irradiation on the blends was investigated by using FTIR. Gel fraction of the irradiated PVP/KC blend contains functional groups of both PVP and KC. All the major functional groups of PVP and KC were present in FTIR spectra of PVP/KC blends (not given

Figure 4. FTIR spectra of (a) PVP, (b) KC, and (c) PVP/KC blend (weight percentage of PVP and KC in blend is 10 and 3, respectively).

TABLE I
FTIR Band Assignments of PVP and KC

Absorption (cm ⁻¹)	Functional Groups
PVP	
2948/2918/2875	CH and CH ₂ stretch
1759	Non-hydrogen bonded νC=O
1679	Non-hydrogen bonded amide νC=O
	Contribution from C=O and N—C stretching
1664	CH deformation of cyclic CH ₂ groups
1492/1459/1419/1371	Amide III band (C—N stretch)
1282/1267	Amide V band or CH ₂ rock
732	Amide IV band
648	
KC	
3400–3000	O—H (stretching)
1380–1355	Sulfates (stretching)
1250–1230	O=S=O (asymmetric stretching)
1045	C—OH + S=O
1010–1080	Glycosidic linkage
	C—O—C (3,6 anhydro-D-galactose) (stretching)
928–933	C6 group in β-D-galactose
900–890	
850–840	C4—O—S in galactose (stretching)

in the text).¹⁸ FTIR results would clearly confirm that KC grafts to PVP after irradiation or forms IPN with PVP. Abad et al.²² proposed that irradiation of KC with γ-rays results in radical formation on the carrageenan macromolecule chains and these sites of radical formation become the points of initiation for side chains with PVP. It is well known that KC degrades very rapidly with irradiation.^{18,23} FTIR spectra of PVP/KC blends, having no change upon 25-kGy irradiation, also indicated that the leakage of KC is inhibited by blending with PVP. Grafting of KC to PVP or

Figure 6. Standard force versus strain (%) curves of the unirradiated and 25-kGy-irradiated PVP/KC/KCl/PEG hydrogel system. Weight percentage of PVP, KC, KCl, and PEG in the mixture is 10, 2, 0.3, and 1.5, respectively.

forming IPN diminished the degradation of KC; or PVP preserved the KC against γ-irradiation.

Mechanical properties of hydrogels

No significant changes were observed in the FTIR spectra of blends upon irradiation. However, blends became mechanically hard and elastic because of their highly crosslinked structure. Figure 6 shows the stress–strain curves of 10% w/w PVP, 2% w/w KC, 0.3% w/w KCl, and 1.5% w/w PEG containing gels before and after irradiation. Unirradiated blend was less stable against compression. Gel strength of the hydrogel increased abruptly with increasing dose

Figure 5. The hydroxyl (OH) (i), and the carbonyl (C=O) (ii) stretching vibrations in (a) pure PVP, (b) 3% PVP and 1% KC, (c) 3% PVP and 2% KC, (d) 3% PVP and 3% KC containing blends, and (e) pure KC.

Figure 7. (a) Standard force versus strain (%) curves of (a) 10% PVP, 0.3% KCl, 1.5% PEG and at various amounts of KC, (1) 1% KC, (2) 2% KC, and (3) 3% KC containing hydrogels. (b) 10% PVP, 2% KC, 1.5% PEG and various amounts of KCl, (1) 0.1% KCl, (2) 0.3% KCl, and (3) 0.5% KCl containing hydrogels (total irradiation dose is 25 kGy).

from 0 to 25 kGy. Although the fracture stress is 30 kPa for the unirradiated sample, it is 1750 kPa for the sample irradiated at a dose of 25 kGy. The fracture strain changes from 0.88 to 3.02 mm with increasing dose. Toughness is 2.13 mJ for the 0-kGy sample and 83.6 mJ for the 25-kGy sample. These results indicate that the radiation dose influences the mechanical behavior of the blend because of increase of crosslinking density of the network. It is well known that network crosslinking density is one of the parameters that controls the mechanical behavior of a gel.

Effect of the KC content on the mechanical properties of blends is given in Figure 7(a) for 10% w/w PVP, 0.3% w/w KCl, and 1.5% w/w PEG containing hydrogels prepared at a dose of 25 kGy. As can be seen from Figure 7(a), increasing the content of KC from 1% w/w to 3 changes all the mechanical properties. This can be explained as the elevation of physical and chemical crosslink densities of hydrogel by irradiation. Effect of KCl on the mechanical properties of 2% w/w KC is represented in Figure 7(b). KC exhibits a weak dependence on potassium concentration. After 0.3% w/w KCl, no change occurred. Because of stoi-

chiometric calculations, it was found that addition of 0.12% w/w KCl is an adequate amount for the complete gelation of sulfate groups in 2% w/w KC.¹⁸ KC was saturated by adding 0.3% w/w KCl to the gelation mixture. Excess of KCl does not affect the physical strength of hydrogel to a significant extent.

Swelling in PECF solution

Preliminary *in vitro* studies in simulated physiological body fluids are very important for the application of hydrogels as biomaterials. Thus, prediction of the behavior of the hydrogel provides a great advantage to a designer from a scientific point of view.²⁴ The accumulation of wound exudate often causes maceration and bacterial overgrowth in the wound site. To prevent a secondary infection of bacteria, an ideal wound dressing absorbs wound fluid.¹⁴

To simulate the absorption of wound fluid, a PECF solution at a pH of 7.4 and with an ionic strength of 0.48M was used. Figure 8(a) and (b) show the percentage swelling of PVP/KC hydrogels after 1-week immersion at room temperature in PECF solution. Figure 8(a) shows the effects of dose and KCl content on the PECF solution adsorption capacity of hydrogels containing 10% w/w PVP, 2% w/w KC, 1.5% w/w PEG, and 0–0.5% w/w KCl. No significant change was observed in the percentage swelling of hydrogels upon irradiation, probably because of the very high ionic strength of the PECF. Except for one hydrogel system, the percentage swelling of hydrogels in PECF changed between 90–110, independent of gel composition.

Effects of KC content on the swelling behaviors of 10% w/w PVP, 1.5% w/w PEG hydrogels with various amounts of KCl in the PECF solution are given in Figure 8(b). Corresponding decreases in the degree of swelling of hydrogels were observed with increasing KC concentration. This decrease is probably attributable to the increase of intermolecular crosslinks in PVP and/or the increase of entanglements by IPN formation in PVP/KC hydrogels. KCl does not influence the percentage swelling of hydrogels in PECF solution.

Acidity/alkalinity (pH) of aqueous extracts

Human skin has an acidic nature that ranges between pH 4 and 6.8. Wound healing is promoted when the pHs of skin and wound are maintained at a slightly lower pH.²⁵ Therefore, the pHs of aqueous extracts of hydrogels should be in this region. Determination of the pH makes it possible to determine the influence of the implanted material on the acid-base equilibrium of surrounding tissues.

As shown in Table II, pHs of extracts of our hydro-

Figure 8. (a) Effect of irradiation dose and the amount of KCl on the swelling behaviors of 10% PVP, 2% KC, 1.5% PEG containing hydrogels in the PECF solution. (b) Effect of KC and KCl content on the swelling behaviors of hydrogels in the PECF solution. The PVP and PEG contents are 10 and 1.5%, respectively, for all hydrogels (total irradiation dose is 25 kGy).

gel systems are <7.50 . Extracts of the hydrogels were found to have pHs ranging from 5.65 to 7.40 after 72 h incubation. These pH values were compared with some commercial dressings and it was observed that our hydrogel systems have a similar pH range to those commercial dressings.²⁶

Electrical conductivity of aqueous extracts

The major components of body fluids, for example, blood plasma, interstitial, and cell fluids are composed of electrolytes, organic substances, and proteins. The electrolytes supply ions that the body needs, help maintain osmotic pressure relationships, and serve as buffers. The sodium ion (with anions such as SO_4^{2-} , HCO_3^- , Cl^- , or HPO_4^{2-}) dominates in both blood and interstitial fluid, whereas the potassium ion dominates inside the cells. The issue of conductivity is important, because it was

TABLE II
Acidity/Alkalinity (pH) of PVP/KC Hydrogels

Hydrogel System	pH
10 PVP/2 KC/1.5 PEG (0 kGy)	5.96
10 PVP/2 KC/0.1 KCl/1.5 PEG (0 kGy)	7.40
10 PVP/2 KC/0.3 KCl/1.5 PEG (0 kGy)	5.89
10 PVP/2 KC/0.5 KCl/1.5 PEG (0 kGy)	6.47
10 PVP/2 KC/1.5 PEG (15 kGy)	5.95
10 PVP/2 KC/0.1 KCl/1.5 PEG (15 kGy)	5.68
10 PVP/2 KC/0.3 KCl/1.5 PEG (15 kGy)	5.81
10 PVP/2 KC/0.5 KCl/1.5 PEG (15 kGy)	5.84
10 PVP/2 KC/1.5 PEG (25 kGy)	5.97
10 PVP/2 KC/0.1 KCl/1.5 PEG (25 kGy)	5.85
10 PVP/2 KC/0.3 KCl/1.5 PEG (25 kGy)	7.10
10 PVP/2 KC/0.5 KCl/1.5 PEG (25 kGy)	6.51
10 PVP/2 KC/1.5 PEG (35 kGy)	7.10
10 PVP/2 KC/0.1 KCl/1.5 PEG (35 kGy)	6.32
10 PVP/2 KC/0.3 KCl/1.5 PEG (35 kGy)	6.01
10 PVP/2 KC/0.5 KCl/1.5 PEG (35 kGy)	5.65

discovered that the more conductive a wound dressing, the greater the analgesic effect of the product.

Electrical conductivity results of aqueous extracts of hydrogels are given in Figure 9. As can be seen from the figure, the electrical conductivity of aqueous extracts increases with irradiation dose. This increase is attributed to an increase of sol fraction with irradiation. As expected, salt addition also increases the electrical conductivity of extracts. Electrical conductivity values of unirradiated mixtures and 15-kGy-irradiated gels are compared in Figure 9. It can be observed that the gelation of the PVP/KC system decreases the electrical conductivity sharply, probably because of decrease of the solubility of gel with crosslinking and decrease of the ion escape ability from the gel structure. Increase of the electrical conductivity with irradiation dose supports this idea.

Figure 9. Variation of electrical conductivity as a function of irradiation dose and KCl content.

Figure 10. Variation of bioadhesion energy with KCl content and irradiation dose.

Bioadhesion of hydrogel dressings

Bioadhesion is generally defined as the ability of a biological or synthetic material to stick to the skin or a mucous membrane. Many adhesive dressings cause secondary injury and pain when peeled off from wounds; this is the result of their strong adhesive property. To prevent this secondary injury, the wound dressing should become less adhesive before peeling. Roos et al.²⁷ investigated a series of blends of high-molecular-weight PVP and low-molecular-weight oligomeric PEG. PVP/PEG blends were referred to in the literature as Pressure-Sensitive Adhesives (PSAs). In some applications, such as wound dressing, transdermal drug delivery systems, PSAs act as adhesives and reservoirs for the drug to be delivered.

Dependence of bioadhesion energy of the hydrogels on the irradiation dose and KCl content in the initial mixture containing 10% w/w PVP, 2% w/w KC, 1.5% w/w PEG, and 0–0.5% w/w KCl is given in Figure 10. The softness of a hydrogel is an advantage in adhesion to the tissue surface, because tissue has a rough surface and undergoes movement. Hydrogels were soft at low irradiation doses, and at low KCl levels. As can be seen from Figure 10, adhesion energy varies depending on both the irradiation dose and the amount of KCl used in the hydrogel preparation. Decreasing the irradiation dose and KCl content increases the adhesion energy, because of softness of the hydrogel. Thus, samples prepared at relatively higher irradiation doses and KCl contents are suitable for dressing applications because of their ability to be peeled off from the wound easily.

CONCLUSION

As a result of all these preliminary laboratory tests, it can be said that PVP/KC/KCl/PEG hydrogel is conve-

nient to be used as a wound dressing. It shows some properties that can meet the requirements of an ideal wound dressing. Not only can it absorb the fluid effectively, exhibit high elasticity, be pleasant in touch and painless on removal, but it also has good mechanical strength and good transparency, allowing observation of the healing process. It is also more flexible and achieves better conformation to the wound surface.

Some of the important prerequisites for the clinical usefulness of a wound dressing are its biocompatibility, prevention against bacterial infection, control over evaporative water loss from the wound surface, and permeability for gases. The second stage of this study is the biological investigation of aqueous extracts *in vitro* and *in vivo*. These studies are still in progress for the whole characterization of PVP/KC hydrogels and the identification of their usability in wound dressing applications.

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