# Synthesis, Characterization and Efficacy of Chemically Crosslinked PVA Hydrogels for Dermal Wound Healing in Experimental Animals

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**ABSTRACT:** In this study, we have investigated the efficacy of crosslinked polyvinyl alcohol (PVA) hydrogel as a wound dressing material, using rat as the animal model. The hydrogel was synthesized by chemical crosslinking of PVA with potassium persulphate and the crosslinking reaction parameters were optimized. The developed hydrogel was found to possess excellent mechanical properties, high water absorption capacity, gel content, and optimum water vapor transmission rate, indicating its ability to act as an effective wound dressing material. The inherent nontoxic characteristics of PVA remained unaltered after crosslinking. The *in vitro* diffusion studies of bovine serum albumin (BSA) as model protein, indicated a relatively slow release of protein resulting from its microencapsulation in the polymeric matrix. For *in vivo* studies, full-thickness excision wounds ($2 \times 2$ cm$^2$) were made on the dorsal surface of rats. The hydrogel was applied on the wound and changed at regular intervals. For comparison of wound healing ability, a radiation crosslinked PVA-based hydrogel, "HiZel" was used as a reference control. The wounds treated with PVA hydrogel healed faster as indicated by an increased rate of wound contraction (16.5 days versus 22.0 in control group). Treatment with "Hizel" led to increase in hydroxyproline in the wound tissue, whereas treatment with PVA hydrogel led to increase in both hydroxyproline as well as hexosamine. This probably provides added strength to the tissue, thereby indicating that PVA hydrogel had higher efficacy than "Hizel". The results suggest that chemically crosslinked PVA hydrogel could be used as an effective wound dressing material. © 2008 Wiley Periodicals, Inc. J Appl Polym Sci 111: 1400–1408, 2009

**Key words:** hydrogels; hydrophilic polymer; swelling; thermal properties; crosslinking; wound healing

## INTRODUCTION

The development of synthetic occlusive wound dressing material is currently an area of great commercial interest. An ideal wound dressing material should be flexible, strong, nonantigenic, permeable to water vapor and metabolites, and be able to cover the wound to prevent bacterial infection. Crosslinked polyvinyl alcohol-(PVA) based hydrogels possess most of the afore-mentioned properties, which make them an ideal candidate as wound dressing material.[1,2] Additionally, these hydrogels also create a moist wound environment which further accelerate the healing process.[3]

PVA can be crosslinked by different physical or chemical methods such as electron beam, γ-irradiation,[4] repeated freeze-thaw cycles, photocrosslinking,[5–7] reacting with bifunctional reagents like boric acid, phenyl boronic acid, dialdehydes, dicarboxylic acids, dianhydrides, acid chlorides, epichlorohydrin, etc.[8–12] However, the crosslinked polymers obtained by the afore-mentioned techniques decompose during long-term use, because of the presence of acetal, ester, or urethane bonding linkages, and their stability is also affected in acidic environments.

The aim of this study was to develop a highly elastic and durable PVA hydrogel film by chemical crosslinking technique. Reaction of PVA with potassium persulphate (concentration range 0.01–0.2% w/v) has been reported to convert the hydroxyl groups present in PVA to ketonic functionalities.[13] However, in the presence of higher concentration of persulphate, free-radical chemical crosslinking of the polymeric chain takes place, and this has not been reported so far. The present investigation was undertaken to give further insight into this reaction with an aim to develop hydrogel films. The PVA hydrogels developed by this technique exhibited excellent mechanical properties, gel content, optimum WVTR, and high water absorption capacity. We also incorporated a model protein, bovine serum albumin (BSA), into the crosslinked PVA hydrogels to evaluate its *in vitro* release pattern. The *in vivo* efficacy of developed hydrogels was studied as wound dressing materials using rat as animal model.

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## EXPERIMENTAL

### Materials

For the preparation of hydrogels, PVA (CDH, India) with a molecular weight of ~ 14,000, degree of saponification of >99 mol %, 20 cp viscosity (4% aqueous solution) was used, without further purification. All other reagents used were of analytical grade. For the purpose of comparison of wound healing ability, a radiation crosslinked PVA based hydrogel, "HiZel" (ABS Medicare Pvt. Ltd., Baroda, India), was used as a reference control.

### Preparation of hydrogels

A 10% w/v aqueous solution of PVA was prepared at 95°C using a rotary evaporator (Heidolph, Laborota-4003). Varying amount of potassium persulphate (0.1–2.50%, w/v) was added to this solution, to induce crosslinking. The reaction was allowed to proceed at 80°C and after 75 min of reaction, the solution was transferred to a leveled Teflon tray and air dried in a laminar flow hood to prepare films of 1 mm thickness. The details of PVA hydrogels prepared along with their sample designations have been listed in Table I.

To characterize the release of a model protein from the hydrogel, two different formulations containing BSA (0.2% or 0.4%, w/v) were prepared. The requisite amount of BSA was added to the reaction mixture after cooling it to room temperature. The mixture was allowed to homogenize and subsequently poured into Teflon trays for drying.

### Characterization of PVA hydrogels

#### Gel content

Gel content, which is an indicator of the insolubility of the crosslinked polymer, was determined by soxhlet extraction of the hydrogel with water. For this purpose, the crosslinked films were allowed to swell in excess water for 20 min. The swollen hydrogels were then subjected to soxhlet extraction for 24 h and then dried to a constant weight under vacuum at 30°C. The percent gel content (Gel %) was calculated gravimetrically using the following formula.[6]

$$\text{Gel } \% = \left(\frac{W_g}{W_0}\right) \times 100$$

where $W_o$ and $W_g$ refer to the weight of dry sample before and after extraction. For determination of gel content of commercial dressing "HiZel," the swollen sample was subjected to soxhlet extraction, and the ratio of the final to initial weight of the swollen gel was calculated to determine the gel content.

**TABLE I**
**Details of Formulations and Their Sample Designation**

| Sample designation | Amount (g) | | | |
|---|---|---|---|---|
| | PVA | $K_2S_2O_8$ | BSA | Water |
| H | 10 | – | – | 100 |
| H-1X | 10 | 0.1 | – | 100 |
| H-2X | 10 | 0.2 | – | 100 |
| H-5X | 10 | 0.5 | – | 100 |
| H-12.5X | 10 | 1.25 | – | 100 |
| H-25X | 10 | 2.5 | – | 100 |
| H-5XP2 | 10 | 0.5 | 0.2 | 100 |
| H-5XP4 | 10 | 0.5 | 0.4 | 100 |

#### Mechanical properties

The mechanical properties of hydrogels, i.e., tensile strength and elongation at break were measured using a tensile strength testing machine (Jragrau Instruments, JRI-TT25). Test specimens with a gauge length of 50 mm and width of 10 mm was cut from the hydrogel sample and subjected to a crosshead speed of 50 mm/min.

#### Molecular weight measurement

A known weight (~ 2 g) of fully dried hydrogel film was immersed in water. After 24 h, the hydrogel film was blotted dry and weighed. The number of active crosslink's was determined using the Flory Rehner equation.[14]

$$-[\ln(1-v_2)+v_2+\chi_1 v_2^2] = V_1 n\left[v_2^{1/3}-\frac{v_2}{2}\right]$$

where, $n$ is the number of active network chain segments per unit volume (mol/cm$^3$), $v_2$ is the volume fraction of the polymer in the swollen mass (density of polymer was taken as 1.27 g/cm$^3$), $V_1$ is molar volume of water (18 mol/cm$^3$), and $\chi_1$ is the Flory-Huggins polymer solvent interaction term (0.49). The molecular weight between the crosslink's ($M_c$) was determined using the following formula

$$M_c = \frac{\rho}{n}$$

#### Fourier transform infrared spectroscopy (FTIR)

The FTIR spectra of the polymer films were recorded in the wavelength range 400–4000 cm$^{-1}$ on a BIO-RAD (FTS-40) spectrophotometer.

#### Thermal analysis

The thermal behavior of dried hydrogel films was investigated using Perkin–Elmer Diamond STG-DTA-DSC in $N_2$ atmosphere (flow rate = 200 mL/min) in the temperature range of 50–450°C. A heating rate of

10°C/min and sample mass of 3.0 ± 0.5 mg was used for each experiment.

### Swelling measurement

For swelling experiments, the vacuum-dried films were immersed in excess water at room temperature (~ 30°C). The samples were removed at various intervals and weighed after removal of surface water with filter paper. The swollen gel was then slowly dried to constant weight. The equilibrium water content (EWC) was calculated according to the following formula.[9]

$$\mathrm{EWC}\% = \left(\frac{W_s - W_d}{W_s}\right) \times 100$$

where, $W_s$ and $W_d$ refer to the weight of the hydrogel in swollen and dried state, respectively.

The stability of the developed hydrogels to hydrolytic degradation was investigated by performing the swelling measurements at different pH values (pH ≈ 2.1, 4.1, 6.0, 8.2, and 10.1). The pH of the solution was adjusted prior to equilibration using hydrochloric acid or sodium hydroxide as required. The swelling study was repeated 10 times after vacuum drying of the swollen sample, and the EWC was determined as mentioned earlier.

### Water vapor transmission rate (WVTR)

The WVTR was determined as per the standard procedure.[15] However, keeping in mind the end use of the hydrogel, the experiment was carried out in an atmosphere of 32% ± 3% relative humidity (RH), maintained by saturated $MgCl_2$ solution at a temperature of 32°C as reported in the literature.[16] The test dish was filled up to 2/3rd of its capacity with water and subsequently capped with the hydrogel specimen. The weight loss of this capped test dish was measured after 24 h, and the WVTR was calculated using the following formula:

$$\mathrm{WVTR}\% = \left(\frac{W_i - W_f}{A \times 24}\right) \times 100\ \%(\mathrm{g/m^2/h})$$

where, WVTR is expressed in $g/m^2/h$, $A$ is the area of bottle mouth ($mm^2$), $W_i$ and $W_f$ are the weight of capped test dish before and after 24 h of incubation under specified RH conditions, respectively.

### Hydrogel protein release

BSA-loaded hydrogel samples of 8 mm diameter were cut out from the films and carefully transferred to empty polypropylene tubes containing 15 mL phosphate buffer saline (PBS; 0.1 *M*, pH 7.4). At specified sample collection intervals, 0.5 mL solution was removed from the test solution and transferred to a sample vial. The test solution was replenished with 0.5 mL fresh PBS. Duplicate hydrogel test samples were analyzed in each experiment. The concentration of protein released was determined by the method of Lowry et al.[17] using BSA as standard. The mass released at time $i$ ($M_i$) was calculated from the following equation[18,19]:

$$M_i = C_i V + \sum C_{i-1} V_s$$

where $C_i$ is the concentration of protein in the release solution at time $i$, $V$ is the total volume of release solution, and $V_s$ is the sample volume (0.5 mL).

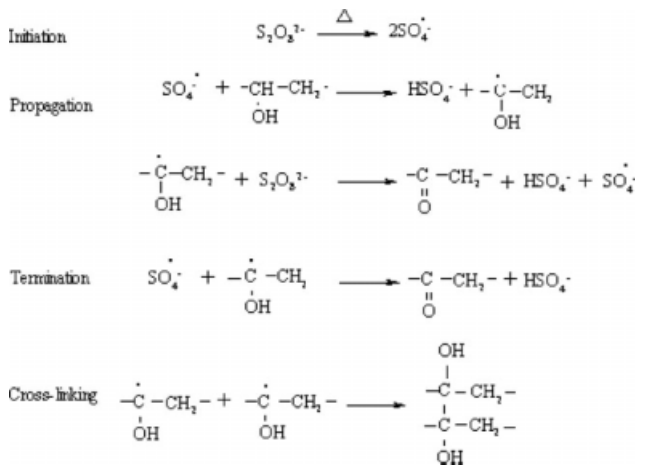
### Surgical procedure and treatment

Male albino rats weighing 190.0 ± 10.0 g were used in this study. The experiments were performed in accordance with regulations specified by the Institute's Animal Ethical Committee and conform to national guidelines on the care and use of laboratory animals. A total of 36 rats were divided into two groups of 18 rats each. Furthermore, control and experimental (H-5X and "HiZel" treated) animals were divided in three subgroups of six rats each. The animals of the first group were used to study rates of wound contraction and epithelialization for 16 days. The animals of the second group were used to study various biochemical and histological changes in the granulation tissue after 7 days of treatment. All hydrogels were sterilized by UV-irradiation prior to animal experimentation.

The animal was anesthetized by intraperitoneal injection of thiopentone (25 mg/kg). The dorsal surface of the rat was shaved, and the underlying skin was cleaned with 70% ethanol. A 2 × 2 $cm^2$ open excision type of wound was created using scalpel blade to the depth of loose subcutaneous tissues. The hydrogels were then applied on the excised wounds and changed daily up to the period of observation. The animals of control group were treated with sterile cotton gauze. The PVA hydrogels were dipped in normal saline for 20 min, prior to application. The dressing material was maintained in position with the help of a microporous tape.

### Biophysical parameters

The rate of wound contraction was initially recorded on Days 4, 8, 12, and 16, and thereafter, on alternate days until healing was completed. The wound surface area was traced on a transparent tracing paper




**Scheme 1** Reaction mechanism of PVA with potassium persulphate.

and measured planimetrically.[20] The period of epithelialization was taken as the number of days required for shedding of eschar without any raw wound left behind.

### Biochemical and histological studies

The granulation tissue collected on 8th day post-wounding was used to assess the biochemical and histological prohealing parameters. The hydroxyproline and hexosamine contents were determined as per established procedures.[21,22] The excised granulation tissue was preserved in 10% neutral formalin. Sections of 6 μm thickness were made and stained with hematoxylin and eosin. Sections were assessed for the histological changes under light microscope in respect of congestion, edema, and infiltration of polymorphonuclear leukocytes, collagen formation, angiogenesis, and epithelialization.

### Statistical analysis

The data has been expressed as Mean ± S.E., and statistical significance between experimental and control values was analyzed by ANOVA followed by Dunnett's *t*-test using Graph Pad Prism 2.01 (Graph Pad Software Inc.). A $P$ value $< 0.05$ was considered statistically significant.

## RESULTS AND DISCUSSION

### Reaction mechanism

Reaction with potassium persulphate lead to the generation of $SO_4^{\cdot-}$ free radicals, which further react to form tertiary radicals on the polymer chain. The reaction mechanism of potassium persulphate with PVA is presented in Scheme 1.[13]

The film obtained after reaction is transparent, however, with increase in the concentration of persulphate, tend to turn slightly yellowish. This can be attributed to the conversion of secondary hydroxyl groups of PVA to >C=O chromophoric functionalities. The insolubility of the final polymer is a result of the reaction between the two macro radicals in the crosslinking step of Scheme 1.

### Characterization of PVA hydrogel

#### Gel content

The variation in gel content with reaction time is presented in Figure 1. It can be seen from Figure 1, that the lowest concentration at which 100% gel content could be achieved corresponds to 0.5% w/v potassium persulphate. The gel content of formulations containing lower concentration of persulphate (<0.5% w/v), reached ~ 60%, after which it leveled off. At higher concentrations (>0.5% w/v), 100% gel content was achieved in slightly lesser time, but considering the additional step which would be required for removal of the unreacted persulphate, 0.5% w/v was chosen as the optimum persulphate concentration. The gel content of the radiation crosslinked sample, "HiZel," was determined to be 100%.

#### Mechanical properties

The investigated mechanical properties i.e., tensile strength, as well as elongation at break was found to depend on the amount of persulphate. As expected, crosslinking led to an improvement in the tensile strength and decrease in percent elongation (Fig. 2). At persulphate concentrations higher than 1.25% w/v, the hydrogels became brittle and broke during handling. Optimum mechanical properties and 100% gel content was achieved with 0.5% w/v,

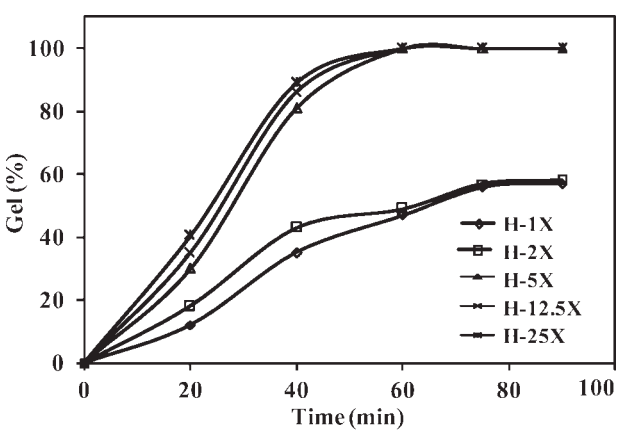



**Figure 1** Variation of gel content of polyvinyl alcohol (PVA) hydrogels with reaction time.

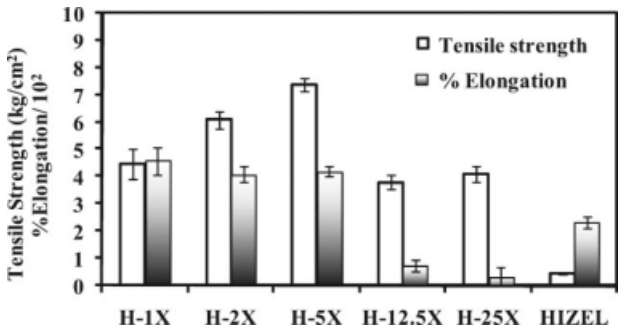



**Figure 2** Variation of tensile strength and elongation of polyvinyl alcohol (PVA) hydrogels due to crosslinking.

persulphate crosslinking (tensile strength of 7.41 ± 0.24 kg/cm$^2$ and elongation of 420% ± 21%), hence *in vivo* wound healing studies were performed using these hydrogel films (H-5X). "HiZel" on the other hand, exhibited a tensile strength of 0.44 ± 0.02 kg/cm$^2$and elongation of 232 ± 20%.

## Molecular weight measurement

From the swelling measurement, the number of active chains ($n$) and the molecular weight between crosslink's ($M_c$) in H-5X hydrogel were calculated, and it was found to be 6.9 × $10^{-4}$ mol/cm$^3$ and 1.8 × $10^3$ g/mol, respectively.

## FTIR

The change in the FTIR spectra of PVA as a result of reaction with persulphate is presented in Figure 3. The spectra of PVA exhibited absorption bands at 3340 cm$^{-1}$ and 1446 cm$^{-1}$ because of O—H stretching and O—H bending. The reaction of PVA with persulphate did not lead to any perceptible changes in the FTIR spectra, besides an enhanced absorption peak at 1713 cm$^{-1}$, which can be attributed to the conversion of the hydroxyl groups of PVA to >C=O functionalities.

## Thermal analysis

The DSC and TGA traces of neat PVA and H-5X in the temperature range of 50–475°C ($N_2$ atmosphere) are shown in Figure 4. From the DSC traces, it is apparent that PVA is a semicrystalline polymer, exhibiting a melting point at 229°C. This is immediately followed by a decomposition step at initial decomposition temperature (IDT) of 240°C, which corresponds to a broad endotherm in the DSC trace. On the other hand, H-5X decomposed prior to reaching the melting temperature and exhibited a double-step decomposition. The IDT was found to decrease with increase in the degree of crosslinking (150°C for H-1X and 143°C for H-25X).

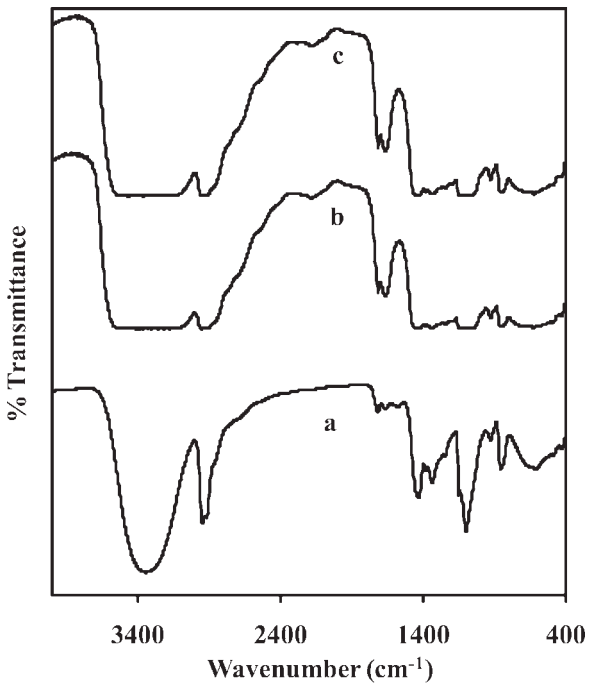



**Figure 3** FTIR spectra of hydrogels (a) PVA, (b) after 40 min of reaction and (c) after 75 min of reaction.

## Swelling studies

The increase in the EWC (%) as a function of immersion time is presented in Figure 5. All the formulations absorbed water rapidly during the initial period and gained equilibrium within 20–30 min of immersion. Moreover, the absorption of water was found to depend on the degree of crosslinking. It is to be noted here that neat PVA films dissolved partially when placed in water, and therefore, their EWC could not be determined.

The EWC of the H-5X was measured under different pH conditions (pH ≈ 2, 4, 6 and 8, and 10) after repeated drying cycles, and the results are presented in Figure 6. It can be seen that there is no change in

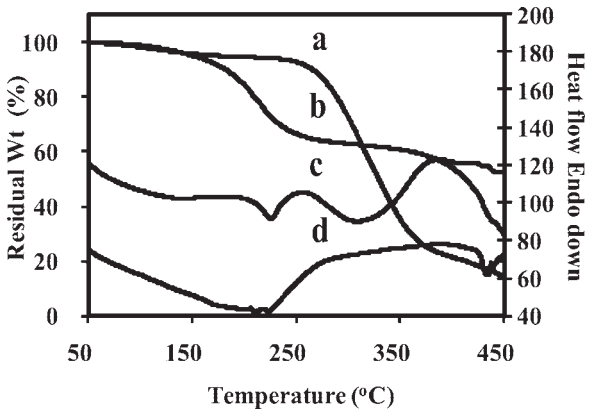



**Figure 4** Thermogravimetric curves (a) PVA, (b) H-5X, DSC curves (c) PVA, and (d) H-5X.

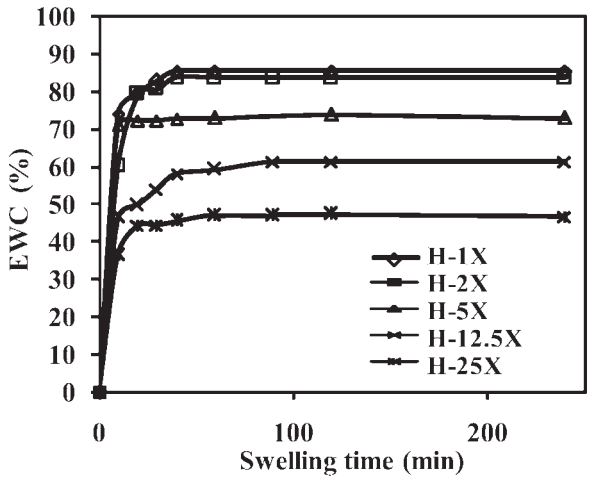



**Figure 5** Relationship between EWC (%) of polyvinyl alcohol (PVA) hydrogels and immersion time (min).

the EWC even after 10 repeated drying and swelling cycles, and the mechanical properties remained unaltered (tensile strength of 7.1 ± 1.1 kg/cm$^2$ and % elongation of 390 ± 10% after 10 cycles), thereby confirming the inherent hydrolytic stability of the hydrogel, which can be attributed to the absence of hydrolysable linkages.

## Water vapor transmission rate

The WVTR of developed PVA hydrogel samples and "HiZel" (32% RH) are presented in Table II. It is apparent that the commercial sample "HiZel" has slightly lower WVTR, 14.0 ± 2.6 g m$^2$ h when compared with 20.0 ± 2.5 g/m$^2$/h for H-5X. WVTR of some commercial wound dressings have been reported to lie in the range of 33–208 g/m$^2$/h.[23] Although there is no available ideal value of WVTR for wound dressings, but the value must not be too high to cause a dry condition in the wound area.[16] On the other hand, if the WVTR value is too low, it will lead to the accumulation of exudates, which opens up the risk for bacterial infection.

**TABLE II**
**Water Vapor Transmission Rate (WVTR) of Developed PVA Hydrogel and "HiZel" Samples**

| Sample | WVTR (g/m$^2$/h) at 32% relative Humidity |
|---|---|
| H-1X | 21.1 ± 2.3 |
| H-2X | 20.2 ± 2.9 |
| H-5X | 20.0 ± 2.5 |
| HiZel | 14.0 ± 2.6 |

## BSA release from hydrogel

Using the BSA release data, the effective diffusion coefficient ($D_e$) of BSA in PBS was analyzed according to established methods.[19] For short-time release ($M_i/M_\infty < 0.6$), Fick's equation is as follows:

$$\frac{M_i}{M_\infty} \cong 2\left[\frac{D_e t}{\pi \delta^2}\right]^{1/2}$$

where, $M_\infty$ is the mass released at time infinity, and $M_i/M_\infty$ is the fractional mass of released BSA. For hydrogels containing BSA (0.2% or 0.4%, w/v), the $M_i/M_\infty$ values were plotted as a function of the square root of release time ($t^{1/2}$) (Fig. 7). It can be seen that most of the BSA was released within 5 h. For calculation of $D_e$, the equation was applied only for the initial region $M_i/M_\infty < 0.6$ i.e., for duration of ~ 110 min. A linear fit of each data was obtained, and $D_e$ was calculated from the slopes. The $D_e$ of BSA in water has been reported to be 8.1 × 10$^{-7}$ cm$^2$/s[24] and the diffusion coefficient, as calculated

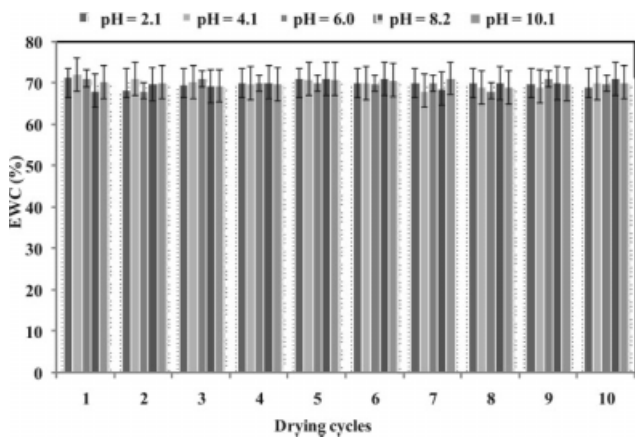



**Figure 6** Effect of pH and drying cycles on the EWC of H-5X.

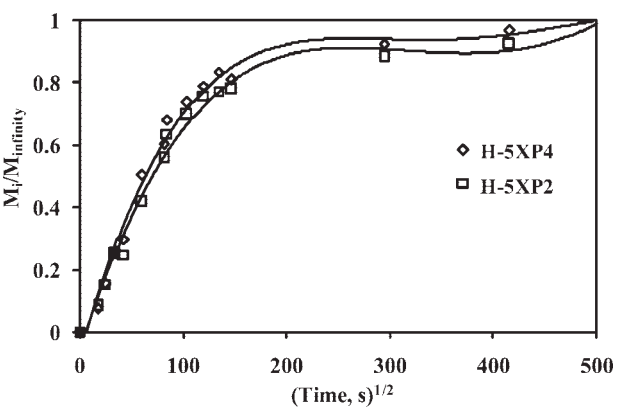



**Figure 7** Release pattern of bovine serum albumin (BSA) from polyvinyl alcohol (PVA) hydrogel as a function of time.

**TABLE III**
**Effect of PVA Hydrogel on Wound Contraction ($mm^2$) and Epithelialization Period**

| Groups | Postwounding days | | | | | Period of epithelialization (days) |
|---|---|---|---|---|---|---|
| | 0th Day | 4th Day | 8th Day | 12th Day | 16th Day | |
| Control | 399.8 ± 22.9 | 339.2 ± 20.5 (15) | 223.7 ± 9.4 (44) | 124.5 ± 9.4 (69) | 55.7 ± 6.4 (86) | 22.0 ± 0.3 |
| PVA Hydrogel (H-5X) | 401.2 ± 6.7 | 283.0 ± 21.8* (29) | 100.7 ± 7.2* (75) | 53.3 ± 6.7* (87) | 3.6 ± 0.2* (99) | 16.5 ± 0.3* |
| HiZel | 401.6 ± 7.2 | 275.0 ± 10.6* (32) | 93.8 ± 4.5* (77) | 49.6 ± 6.2* (88) | 3.3 ± 0.2* (99) | 16.2 ± 0.3* |

Values are mean ± S.E. for six animals; Numbers in parenthesis indicate percentage of wound contraction.
* $P < 0.01$ compared with control.

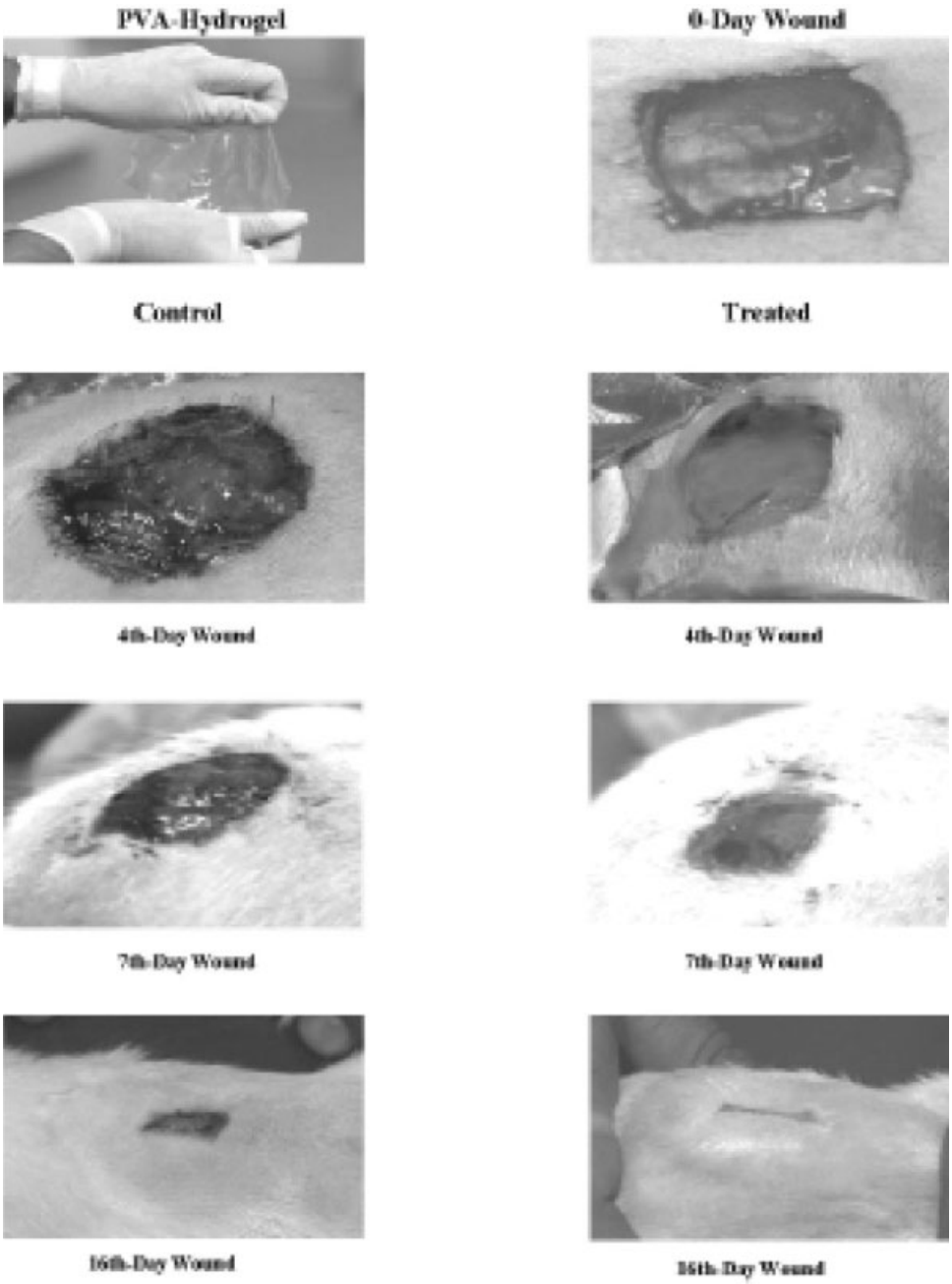



**Figure 8** Photographical representation of wound contraction rate on different days of postwounding (0, 4, 7, 16) of control animal treated with cotton gauze and experimental animals treated with PVA hydrogels exhibiting average wound healing pattern in control animals, whereas PVA hydrogel treated wounds exhibiting faster healing pattern.

**TABLE IV**
**Effect of PVA Hydrogel Application for 7 Days on Prohealing Parameters in Granulation Tissues**

| Groups | Hydroxyproline (mg/g tissue wt.) | Hexosamine (mg/g tissue wt.) |
|---|---|---|
| Control | 21.04 ± 1.20 | 0.68 ± 0.03 |
| PVA Hydrogel (H-5X) | 28.93 ± 0.83* | 0.88 ± 0.03* |
| HiZel | 25.53 ± 0.70* | 0.71 ± 0.03 |

Values are mean ± S.E. for six animals.
* $P < 0.01$ compared with control.

from the slopes (Fig. 7) was found to be $1.2 \times 10^{-8}$ and $4.2 \times 10^{-8}$ $cm^2/s$ for 0.2% and 0.4% BSA (w/v), respectively. This decrease in the diffusion coefficient of the BSA in PVA is indicative of the microencapsulation of the BSA in the polymeric matrix, which in turn is responsible for its relatively slow release.

### Efficacy of PVA hydrogel on experimental wounds

Visual observation of the animals treated with PVA hydrogel showed moist wound, with no clinical sign of inflammation or any pathological fluids oozing out from the wound margins. The PVA hydrogel treated animals showed a significant ($P < 0.01$) improvement in the rate of wound contraction, which was comparable with that of the reference control i.e., "HiZel" dressing-treated group of animals (Table III). The photographic evaluation clearly indicated a faster healing of the wounds in the experimental animals (Fig. 8). The epithelialization and complete closing of wounds was observed by 16th day for animals treated with PVA and 22nd day for the sterile-gauze-treated control animals (Table III). The levels of hydroxyproline and hexosamine were found to be significantly higher in the PVA hydrogel treated group, when compared with "HiZel" and control group, suggesting that developed PVA hydrogel had higher efficacy than "Hizel" (Table IV). Hydroxyproline, the main constituent of collagen serves as a marker of collagen biosynthesis at the wound site and hexosamine level reflects the stabilization of collagen molecules by enhancing electrostatic and ionic interactions. Collagen not only confers strength and integrity to the tissue matrix but also plays an important role in homeostasis and in epithelialization at the later phase of healing. The histological examinations revealed that tissue regeneration was much greater in wound treated with PVA hydrogel and "HiZel" treated groups (Fig. 9) without any signs of necrosis, edema, congestion, or inflammatory changes. More relative fibrosis and reepithelialization were observed in PVA hydrogel treated wound.

## CONCLUSIONS

The developed PVA hydrogel (H-5X) exhibited excellent mechanical properties, gel content, high water absorption capacity, and optimum WVTR. The crosslinking agent, potassium persulphate did not adversely affect the biocompatibility of the developed PVA hydrogels. The biochemical parameters and histological examinations have shown that the PVA-hydrogel-treated wounds healed much faster than the wounds of control animals treated with sterile cotton gauze. The PVA-hydrogel-treated wounds closed completely on the 16th day when

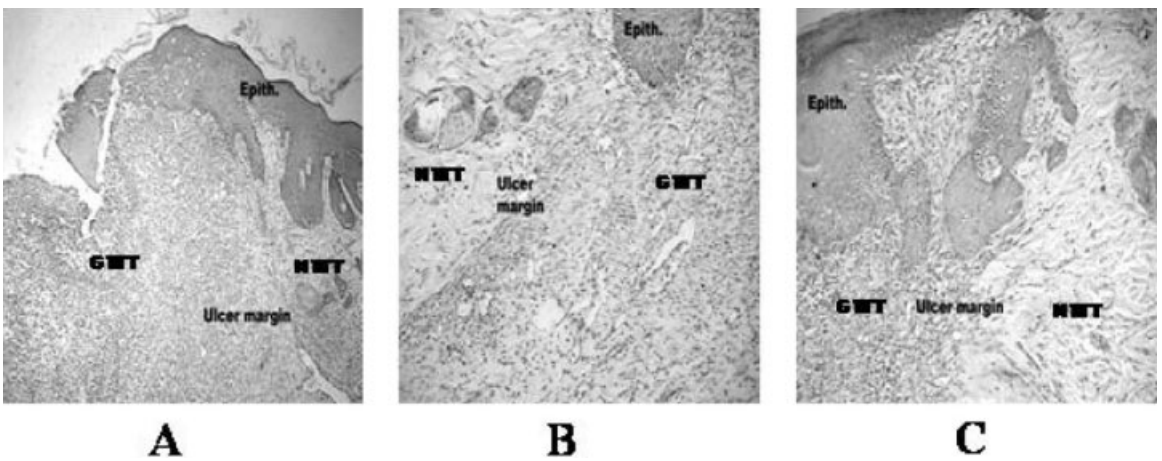



**Figure 9** Photomicrograph of the dermal region showing the interface between granulation wound tissue (GWT) and nonwounded healthy skin (NWT) on 7 day postwounding (A) wound tissue of control animal with incomplete epithelialization and infiltration of inflammatory cells, (B) wound tissue of polyvinyl alcohol (PVA) hydrogel treated animal with greater degree of epithelialization and fibroblastic deposition, (C) wound tissue of "HiZel" treated animal with on-going epithelialization and fibroblastic deposition (H and E, ×4).

compared with the wounds of control animals on the 22nd day. The results clearly indicate that chemically crosslinked PVA hydrogel film could be used as an effective dressing material for wound healing.

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