

DEHYDRATION KINETICS OF POLYVINYL ALCOHOL HYDROGEL WOUND DRESSINGS DURING WOUND HEALING PROCESS

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Abstract The hydrogel wound dressing based on polyvinyl alcohol (PVA) was prepared by the freezing-thawing cyclic method. The dehydration kinetics of prepared hydrogels was determined using the experimental method and mathematical modeling based on diffusion mechanism. The results show that the dehydration rate of PVA hydrogel wound dressing inversely depends on the hydrogel thickness as well as water content of the wound. On the other hand, the initial water content of hydrogel and the atmospheric humidity have little direct effect on the dehydration rate. The good agreement between experimental and mathematical modeling results in early stages of dehydration process shows that the predominate factor determining the dehydration of these wound dressings is diffusion.

Keywords: Polymer gels; Wound dressing; Polyvinyl alcohol; Dehydration kinetics.

INTRODUCTION

It is well known that wound healing is a complicated proceeding of cellular and biochemical events, which can be accelerated using special medical devices such as wound dressings^[1]. Wound dressings are usually used to encourage the various stages of wound healing process and create better healing conditions. They often cover the wound surface to accelerate its healing process^[2]. Based on the types of wounds and modes of healings, numerous materials and biomaterials have been developed for use as wound dressing^[3, 4]. Among them, special attention has been paid to hydrogels due to their unique interesting properties which can meet the essential requirements of ideal wound dressings including: immediate pain control, easy replacement, transparency to allow healing follow up, absorb and prevent loss of body fluids, barrier against bacteria, oxygen permeability, good handling, control of drug dosage and so on^[2, 5].

PVA hydrogel is one of the well-known polymer hydrogels with good biocompatibility which has been used with numerous research groups as wound dressings in wounds management. Yoshii *et al.* prepared PVA hydrogel wound dressings by combination of electron beam irradiation and acetalization of PVA. They found some advantages of these hydrogel wound dressings over a gauze dressing such as homogeneous adhesion to the affected parts, easy removal without damage to renewed skin and slightly faster rate of reconstruction of the injured skin^[6]. Yoshii *et al.* also prepared PVA and polyethylene oxide (PEO) hydrogels for wound dressing using electron beam irradiation method. The PEO/PVA hydrogel blend showed satisfactory properties for wound dressing based on *in vivo* study on marmot as animal model^[7]. Razzak *et al.* prepared PVA and polyvinyl pyrrolidone (PVP) blended hydrogels for wound dressing using gamma ray irradiation technique. According to

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in vitro assessment it was found that the PVA/PVP blended hydrogel was very useful material that can meet the efficacy requirement and its healing rate was comparable with sterilized gauze and sofratulle. Their obtained results also showed that these hydrogel wound dressings could be considered as good barrier against microbes^[8]. Varshney prepared radiation processed PVA-polysaccharides hydrogels without any synthetic plasticizers and additives for wound dressing applications. Clinical trials of wound dressing on human patients established safety and efficacy of the dressing. The dressing was observed to be useful in treating burns, non-healing ulcers of diabetes, leprosy and other external wounds^[9]. Hong prepared a novel wound dressing material by electrospinning PVA/AgNO₃ aqueous solution into nonwoven webs and then treating the webs by heat or UV radiation. It was found that the only heat treated electrospun PVA/AgNO₃ fiber web was a good material as wound dressings because it had structural stability in moisture environment as well as excellent antimicrobial ability and quick and continuous release of the effectiveness^[10]. Gupta *et al.* investigated the efficacy of crosslinked PVA hydrogel with potassium persulphate as crosslinker for wound dressing applications. 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^[11]. In recent years, a novel class of hydrogel wound dressings, so called as nanocomposite hydrogel wound dressings, was introduced by Kokabi, Hassan and one of us^[2]. These nanocomposite hydrogels were prepared on the basis of PVA and organically modified montmorillonite as nanoclay. The *in vitro* studies showed that PVA nanocomposite hydrogels could meet the essential requirements for the reasonable wound dressing with some desirable characteristics such as relatively good swelling, appreciated vapor transmission rate, excellent barrierity against microbe penetration and mechanical properties. It was also indicated that the quantity of the nanoclay added to the PVA nanocomposite hydrogel is the key factor in obtaining such suitable properties required for wound dressing^[2].

In general, there are various methods for crosslinking in order to produce PVA hydrogels, including electron beam irradiation^[12], bulk mixing with crosslinking agents such as glutaraldehyde and also freezing-thawing cyclic process^[13–15].

In an ideal condition, a desirable hydrogel wound dressing should create and keep a moist environment on the wound surface. The dried hydrogel loses its functionality as effective wound dressing and must be replaced by a fresh one. The replacement time intervals of the hydrogel wound dressings can be determined by calculating their dehydration period. Therefore, having information about the dehydration kinetics of the hydrogel wound dressings would be required. In some previous experimental researches it has been shown that the dehydration kinetics of some hydrogel wound dressings (*e.g.* polyvinyl pyrrolidone and polyethylene glycol) is mainly affected by the water diffusion mechanism^[16].

We have previously investigated the dehydration kinetics of the PVA hydrogel wound dressings during the pre-usage (storage) period, based on the mathematical modeling and experimental studies^[17]. In this work, the hydrogel wound dressings based on PVA were prepared by the freezing-thawing cyclic process and their dehydration kinetics during the wound healing process were investigated by the experimental method and mathematical modeling based on the diffusion mechanism.

MATHEMATICAL MODELING

Consider a sheet of hydrogel wound dressing with a thickness of L having the initial water concentration of c_0 which has been exerted to the wound surface having exudates with water concentration of c_w (Fig. 1). It is also assumed that the top surface of the hydrogel ($x = L$) is exposed to the environment with moisture concentration of c_e .

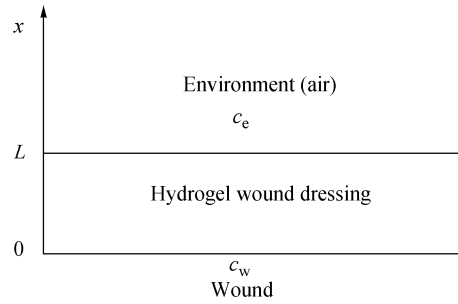


Fig. 1 The wound dressing and its boundaries

In order to investigate the dehydration kinetics of this hydrogel wound dressing during the healing process of wound, we can use the Fick's second law in Cartesian coordinates. The main assumptions made to this purpose are as follows:

- (1) The water diffusion is the dehydration rate controlling step rather other phenomena such as hydrogel swelling and polymer chains relaxation.
- (2) The water diffusion process is one-dimensional and occurs in the smallest dimension of the hydrogel (*i.e.* in x direction).
- (3) The diffusion coefficient of water in hydrogel (D) is constant and independent of concentration.
- (4) The concentration of water in wound exudates (c_w) and air (c_e) are assumed to be constant, during the healing process.

Under these circumstances, the concentration of water inside the hydrogel wound dressing ($0 \leq x \leq L$) is expressed as a function of position variable and time (x, t) and can be determined by the transient diffusion according the Fick's second law, as follows:

$$\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} \quad 0 \leq x \leq L \quad t \geq 0 \quad (1)$$

where, c is the concentration of water inside the hydrogel. The initial and boundary conditions are:

$$c(x, 0) = c_0 \quad (2)$$

$$c(0, t) = c_w \quad (3)$$

$$c(L, t) = c_e \quad (4)$$

Equation (1) is a linear partial differential equation (PDE) having non-homogeneous boundary conditions, which might be solved using the method of separation of variables (product method). Its final solution is as follows:

$$c(x, t) = c_w + \left(\frac{c_e - c_w}{L} \right) x + \sum_{n=1}^{\infty} F_n \sin(\lambda_n x) e^{-D \lambda_n^2 t} \quad (5)$$

where, F_n and λ_n are constants which can be calculated by the following equations:

$$F_n = 2 \left[\left((-1)^n - 1 \right) \left(\frac{c_w - c_0}{n\pi} \right) - \frac{L}{n\pi} (-1)^n \right] \quad n = 1, 2, 3, \dots \quad (6)$$

$$\lambda_n = \frac{n\pi}{L} \quad n = 1, 2, 3, \dots \quad (7)$$

The rates of water diffusion from both sides of the hydrogel (J_1 at $x = 0$ and J_2 at $x = L$) could be expressed based on the Fick's first law:

$$J_1 = \frac{dM_{t1}}{dt} = -DS \frac{\partial c(0, t)}{\partial x} \quad (8)$$

$$J_2 = \frac{dM_{t2}}{dt} = -DS \frac{\partial c(L, t)}{\partial x} \quad (9)$$

where, S is the surface area of the hydrogel. M_{t1} and M_{t2} are the cumulative amounts of water released from the lower and upper sides of hydrogel at time t , respectively. Inserting Eq. (5) in Eq. (8) and Eq. (9) and integrating from 0 to t , gives the M_{t1} and M_{t2} , respectively as:

$$M_{t1} = S \left[\frac{D(c_w - c_e)}{L} t + \sum_{n=1}^{\infty} \frac{F_n}{\lambda_n} (e^{-D\lambda_n^2 t} - 1) \right] \quad (10)$$

$$M_{t2} = S \left[\frac{D(c_w - c_e)}{L} t + \sum_{n=1}^{\infty} \frac{F_n \cos(\lambda_n L)}{\lambda_n} (e^{-D\lambda_n^2 t} - 1) \right] \quad (11)$$

The total cumulative amount of water loss of the hydrogel at any time t (M_t) can be determined by subtracting the Eq. (10) from Eq. (11):

$$M_t = S \left[\sum_{n=1}^{\infty} \frac{F_n}{\lambda_n} (\cos \lambda_n L - 1) (e^{-D\lambda_n^2 t} - 1) \right] \quad (12)$$

The initial amount of water inside the hydrogel (at $t = 0$) or the removed amount at infinite time (M_{∞}) is given by:

$$M_{\infty} = c_0 SL \quad (13)$$

Finally, the fractional release of water at time t is obtained by dividing Eq. (12) to Eq. (13):

$$\frac{M_t}{M_{\infty}} = \frac{1}{c_0 L} \sum_{n=1}^{\infty} \frac{F_n}{\lambda_n} (\cos \lambda_n L - 1) (e^{-D\lambda_n^2 t} - 1) \quad (14)$$

EXPERIMENTAL

Materials

The commercial grade PVA having a degree of polymerization of 1700 and a saponification value of greater than 98% was purchased from the Nippon Synthetic Chemical Industry Co., Ltd, Japan. Double distilled water (DDW) was used to prepare all aqueous solutions.

Preparation of PVA Hydrogel Wound Dressings

PVA hydrogels were prepared by repeatedly cyclic freezing-thawing process. For this purpose, aqueous solutions containing 10%–30% by weight PVA were used. These solutions were mixed slowly and heated up to 90°C for a period about 4 h to achieve complete dissolution. Then the aqueous solutions were poured into plastic moulds and placed at −20°C for 24 h to induce crystallization. After the freezing process, they were subsequently allowed to thaw for 24 h at room temperature. This cyclic process was repeated three times for each sample. The final hydrogel films had various thicknesses of 1, 2, 3, 4 and 5 mm and water contents of

70 wt%, 75 wt%, 80 wt%, 85 wt% and 90 wt% (water concentration of 41.8, 42.2, 46.6, 48.9 and 51.2 kmol/m³, respectively).

Wound exudates solutions were simulated by adding adequate amount of human plasma to DDW. The obtained solutions had the water contents of 0 wt%, 20 wt%, 40 wt%, 60 wt% and 80 wt% (water concentration of 0, 11.6, 22.9, 34.1 and 44.9 kmol/m³, respectively).

Dehydration tests were performed in a constant temperature-humidity chamber (Giant Force Instrument, GTH-072TR, Taiwan). Each simulated wound exudates solutions were poured in a flat plate and the hydrogels were put on the surface of the solution, exposed to air. The experiments were performed at constant temperature (37°C) and various humidity including; 0 wt%, 10 wt%, 20 wt%, 30 wt% and 40 wt% (water vapor concentration of 0, 0.01, 0.02, 0.03 and 0.04 kmol/m³, respectively). The dehydration kinetics of all samples was determined gravimetrically by weighing their weight at some predetermined time intervals.

RESULTS AND DISCUSSION

The dehydration kinetics of PVA hydrogel wound dressings was investigated using both mathematical and experimental methods. For this purpose, the effects of some key characteristic parameters of the hydrogel (*i.e.* thickness and initial water content) and also environmental conditions (*i.e.* water concentration at the wound surface and air humidity) on the dehydration kinetics of PVA hydrogel wound dressing were investigated. The mathematical dehydration curves of hydrogels (*i.e.* the M_t/M_∞ versus time) were plotted at various levels of characteristic parameters such as; hydrogel thickness (L), initial water content of hydrogel (c_0), water concentration at the wound surface (c_w) and air humidity (c_e), using the Eq. (14). In all cases, the diffusion coefficient of water in hydrogel was considered constant as $D = 2.1 \times 10^{-11} \text{ m}^2/\text{s}$ ^[17]. The experimental data were also presented by plotting the measured values of the fractional release of water from the hydrogel (M_t/M_∞) against time for the various levels of the experimental parameters (L , c_0 , c_w and c_e).

Figure 2 demonstrates the effect of PVA hydrogel wound dressing thickness on the dehydration kinetics, from mathematical and experimental viewpoint. Experimental data are the results of five tests done on hydrogels having various thicknesses (*i.e.* 1, 2, 3, 4 and 5 mm) at identical initial water content ($c_0 = 80\%$). Both sides of the hydrogels were kept completely dry ($c_w = c_e = 0 \text{ wt}\%$). Mathematical curves were also plotted at the same experimental conditions for all five samples. Figure 2 shows that the thinner wound dressing exhibits higher value of M_t/M_∞ in comparison with the thicker one at any arbitrary time of dehydration. In other words, it implies that the thinner wound dressing will be dried more rapidly than thicker one. Therefore, in practical usage one must use the thicker PVA hydrogel wound dressing for the wounds with the long period of healing (*e.g.* for chronic or full thickness wounds) to prevent the undesired rapid drying of the dressing in healing process and increase the replacement time intervals of the wound dressing. Figure 2 reveals that the experimental data are in good agreement with the theoretical results, particularly for the early stages of the dehydration process.

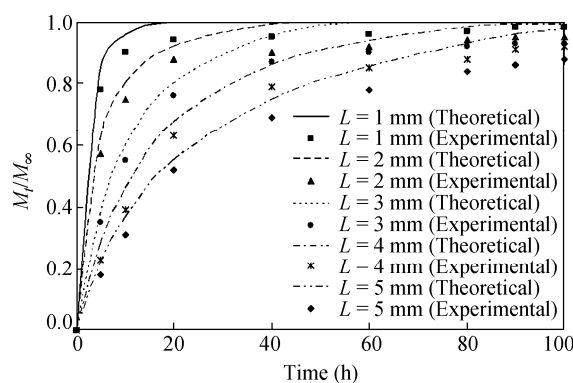


Fig. 2 The effect of wound dressing thickness on dehydration kinetics

The effect of the initial water content of PVA hydrogel wound dressings on dehydration kinetics was shown in Fig. 3. Experimental data were obtained from five tests done on hydrogels having different initial water contents (*i.e.* 70 wt%, 75 wt%, 80 wt%, 85 wt% and 90 wt%) with identical thickness ($L = 3$ mm). Both sides of the hydrogels were again kept completely dry ($c_w = c_e = 0$ wt%). Mathematical curves were also plotted in the same experimental conditions for all samples. Both experimental and theoretical results show that the initial water content of PVA hydrogel wound dressing has minor effect on dehydration kinetics, *i.e.* by raising the value from 70 wt% to 90 wt% no drastic change could be observed in the M_t/M_∞ curves versus time. However, the obtained results show a direct relationship between the initial water content of the hydrogel and its dehydration time.

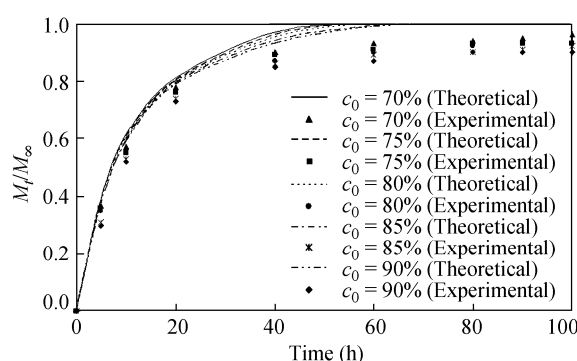


Fig. 3 The effect of initial water content of wound dressing on dehydration kinetics

Figure 4 exhibits the dehydration curves of PVA hydrogel wound dressing against time for various types of wounds, *i.e.* various amounts of wound exudates or water concentration on wound surface. To investigate the effect of water concentration of wound on the dehydration rate of wound dressing, five identical specimens of PVA hydrogels having the same thickness of 3 mm, and identical initial water content of 80 wt% were examined. The upper side of each hydrogel was exposed to completely dry air ($c_0 = 0\%$) and the other side was kept in contact with the simulated wound exudates solution with various water concentrations, *i.e.* 0 wt%, 20 wt%, 40 wt%, 60 wt% and 80 wt%. Mathematical curves were also plotted in the same experimental conditions for all samples. Figure 4 shows that the dehydration rates of PVA hydrogel wound dressings exhibit relatively high dependency to the water concentration of wound. As observed, the dressing exerted to the completely dry wound (non-exudative wound), *i.e.* $c_w = 0\%$, has the highest drying rate in comparison with the other wounds, and by increasing the water concentration up to 80 wt%, the drying rate of dressing decreases. Based on the obtained results, it is clear that the period of the drying of PVA hydrogel wound dressing used for wounds with higher values of exudates is longer than that with lower values. Therefore, the dressings applied to the dry or low exudative wounds will be dried rapidly and required more fresh dressing replacements. Figure 4 also shows nearly good agreement between experimental and mathematical results, especially for the early stages of the dehydration process.

Figure 5 shows the effect of air humidity (water concentration in air) on dehydration kinetics of PVA hydrogel wound dressings. Experimental data are the results of five tests done on identical specimens of PVA hydrogels having the thickness of 3 mm at certain initial water content ($c_0 = 80\%$). The lower side of each hydrogel was kept completely dry ($c_w = 0\%$), while the upper one was in contact with air having various moisture contents, *i.e.* 0 wt%, 10 wt%, 20 wt%, 30 wt% and 40 wt%. Mathematical curves were also plotted at the same experimental conditions for all five samples. As Fig. 5 shows, according to both the theoretical and experimental results, the M_t/M_∞ curves versus time of all samples have little dependency to the air humidity. However, results show that the dehydration time of hydrogel increases by any increment in the air humidity. It means that the atmospheric condition (*i.e.* humidity) has little influence on the drying rate of the PVA hydrogel

wound dressing, but it is evident that the drying of the wound dressing in moist regions will be occurred relatively slower and dressing replacement time intervals broadened.

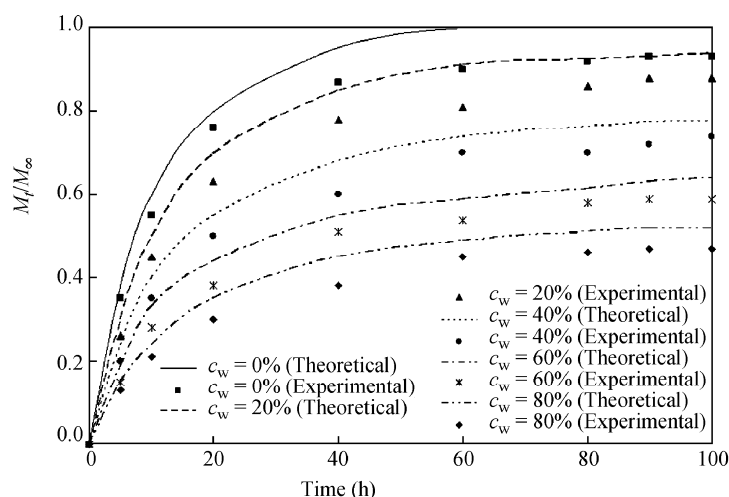


Fig. 4 The effect of wound water content on dehydration kinetics of the dressing

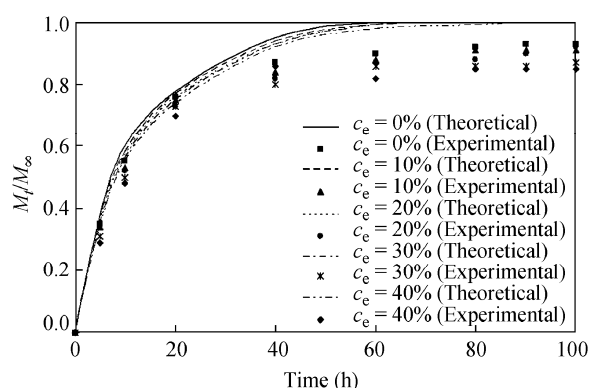


Fig. 5 The effect of air humidity on the dehydration kinetics of the dressing

CONCLUSIONS

In this work, PVA hydrogels were prepared and their dehydration kinetics as wound dressings was investigated based on experimental and mathematical methods. The obtained results show that the dehydration rate depends inversely to the hydrogel thickness and water content of wound. On the other hand, the initial water content of hydrogel and the atmospheric humidity have little direct effect on the dehydration rate. Comparison the theoretical data obtained from the mathematical modeling with the experimental results shows a relative difference between the experimental results and theoretical data, particularly in higher times of dehydration process. It seems that this difference arises from the fact that the effect of the evaporation of water from the upper side of the dressing was not assumed in the mathematical modeling of the dehydration process of the wound dressings. However, the results obtained from the mathematical modeling based on diffusion mechanism in early stages of dehydration process were in good agreement with the measured experimental results. So, it can be concluded that the main phenomenon governing the dehydration of PVA hydrogel wound dressings is diffusion.

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