

Swelling Properties of Propranolol HCl-loaded Polyvinyl Alcohol-*graft*-lactic Acid Hydrogel Films

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Abstract. This paper presented the swelling properties of propranolol HCl-loaded polyvinyl alcohol-*graft*-lactic acid (PPH-loaded PVA-*g*-LA) hydrogel films. The swelling properties including swelling-deswelling measurement and swelling behaviour in different environmental stimuli fluids such as water, various pH, and various ionic strength were determined. It was found that the swelling properties of the PPH-loaded PVA-*g*-LA hydrogel films depend on the LA amount addition. They had a good swelling and deswelling in water and acetone. The PPH-loaded PVA-*g*-LA hydrogel films showed the high swelling in the medium pH 7. Thus, the prepared PPH-loaded PVA-*g*-LA hydrogel films had a good swelling property that could be used to controlled drug release in pharmaceutical product.

1 Introduction

The adhesive hydrogel films are polymer networks holding a significant amount of water whilst maintaining their structural integrity without dissolution whereas such thin films are adhering on human skin. They are ideal biocompatible materials that can be used as adhesives for several technologies and applications. They will be providing the controlled drug release from their formulation ; as well as, the active drugs can easily diffuse and through-out from the adhesive hydrogel films. The adhesive hydrogel films can be prepared by two method, chemical and physical hydrogel films that are replaced the hydrogen bond as cross-linked networks by intramolecular and prevented by physical interactions between different more than two polymer chains by intermolecular, respectively [1-5].

Polyvinyl alcohol (PVA) is hydrolyzed from polyvinyl acetate and produced a high percentage of repeat units which is mainly composed of C–C bonds with pendant hydroxyl groups. It is a water-soluble polymer, low toxicity, and biodegradable. It can be modified by chemical reaction and blending such as grafting with starch [6], blending with methylated cornstarch-based film [7], blending with modified xylan [8], and crosslink with maleic acid [9]. In addition, modified PVA hydrogel can be desired as a hydrophilic polymer that can accordingly swell or shrink in water or environmental stimuli fluids such as pH, temperature, ionic strength, etc. PVA hydrogels have become especially attractive to the various fields such as pharmaceutical, biomedical, and tissue engineering including ophthalmic contact lenses, drug delivery, and tendon repair [10]. Lactic acid (LA) is a wide

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availability and relatively low cost that commonly used in biomaterial applications. The LA can be grafted with hydroxyl groups of PVA by esterification method may decrease the hydrophilicity, and intra- and intermolecular hydrogen bonds of the PVA. The reactions between alcohols of PVA and carboxylics of lactic acid can take place with catalysts at various temperatures. For example, the grafting on backbone of PVA with a copolymer of lactide and glycolide by ring-opening melt polymerization using stannous octoate as catalyst is reported by Breitenbach and Kissel [11]. Their physicochemical properties, such as melting point, glass transition point, degree of crystallinity, molecular composition and architecture, could be systematically adjusted as new class of biodegradable polymers to the considerable potential as drug delivery. Moreover, the PVA-*graft*-LA (PVA-*g*-LA) is fully soluble in cold water and improving flexibility and elasticity as well as tear resistance when it is synthesized by melt polymerization at 100°C under nitrogen atmosphere and continuously stirred [12], using stannous chloride [13], stannous 2-ethyl hexanoate [14], and manganese acetate [15] as a catalyst. However, the previous reports of PVA-*g*-LA reaction have been carried out under organic solvents, initiator, and catalysts that are environmental concerns and high cost and react under nitrogen atmosphere. Therefore, the present research focused on a green route synthesis has not yet been reported for the grafting reaction of LA onto PVA in a water-based system. The green route synthesis is prepared by eco-friendly curing method which is a one term of polymer chemistry and polymer process engineering without chemical agents.

Our previous publication reported the thermal properties including differential scanning calorimetry and thermogravimetric analysis, the confirmation of main functional groups by Fourier transform infrared spectroscopy, the swelling-deswelling behavior, and the moisture measurement per dry mass of modified polyvinyl alcohol-*graft*-lactic acid (PVA-*g*-LA) hydrogel films that synthesized by eco-friendly synthesis method [16]. Presently, we studied the preparation of the propranolol HCl (PPH)-loaded PVA-*g*-LA hydrogel film. The hydrogel films were synthesized in aqueous solutions without initiator and catalyst. The different amounts of PVA and LA were 1:0.5, 1:1, 1:1.5, and 1:2, and different curing times were 120, 150, and 180 min at 100°C. The swelling behaviors were characterized by swelling-deswelling measurement and swelling behavior in different environmental stimuli fluids such as water, various pH, and various ionic strength.

2 Experimental Works

The compositions of PPH-loaded PVA-*g*-LA hydrogel films are also shown in Table 1. Firstly, PVA ($M_w = 195,000$ g/mol) was dissolved in ultrapure water by heating it on a water bath at $70 \pm 2^\circ\text{C}$ and being continuously stirred until clearly PVA solution. Subsequently, it was cooled down to room temperature. 80% L-(+)-LA solution was slowly added into clearly PVA solution with the help of a mechanical stirrer for 60 min to form a homogeneously gel-like mixture solution. The PPH powder was mixed in the mixture. After that, the gel-like mixture solution was cured at high temperature in an oven.

The swelling-deswelling behaviors, area $2\text{ cm} \times 2\text{ cm}$ of PPH-loaded PVA-*g*-LA hydrogel films were immersed in excess distilled water at room temperature and then swollen samples were weighted (W_s). Then, swollen PPH-loaded PVA-*g*-LA hydrogel films were transferred into acetone at room temperature and were weighted at time interval (W_n) until equilibrium point. The reswelling and deswelling behaviors were measured again in distilled water and acetone, respectively at room temperature. The swelling or reswelling was calculated in terms of the relative gel volume (V_{rel}) using the following equation (1) [17].

$$V_{rel} = (W_n / W_s)^3 \quad (1)$$

Table 1. Ingredient composition and preparation conditions of PPH-loaded PVA-g-LA

Code	PVA (g)	LA (g)	PPH (g)	Water (g)	Temperature (°C)	Time (min)
PL1	5.0	2.5	5.0	87.5	100	120
PL2						150
PL3						180
PL4		5.0		85.0	100	120
PL5						150
PL6						180
PL7		7.5		82.5	100	120
PL8						150
PL9						180
PL10		10.0		80.0	100	120
PL11						150
PL12						180

The 1.0-1.5 g of PPH-loaded PVA-g-LA hydrogel films were placed on aluminum pan and then heat at 120°C. The percentage of moisture content was measured by moisture analyzer (model: MAC 50/NH, Poland) and calculated according to equation (2).

$$\text{Moisture content (\%)} = (W_{\text{initial}} - W_{\text{dry}}) / W_{\text{initial}} \quad (2)$$

Swelling measurement of PPH-loaded PVA-g-LA hydrogel films were investigated the effect of pH and different cations. Various pH preparations were adjusted to 2, 4, 7, and 10 using 1 mol/L sodium hydroxide and 1 mol/L hydrogen chloride aqueous solution in distilled water. The 10 mmol/L chloride salt of sodium chloride or potassium chloride were prepared as swelling media. Then, the samples were immersed in swelling media at time intervals. The equilibrium swollen samples were weighted and calculated according to equation (3). The all data were reported.

$$\text{Ratio of water absorption amount} = (W_2 - W_1) / W_1 \quad (3)$$

where W_1 was dried sample and W_2 was swollen sample.

3 Results and discussion

The swelling-deswelling behaviors of the PPH-loaded PVA-g-LA hydrogel films were determined in distilled water and acetone that are shown in Figure 1. The deswelling behavior of swollen PPH-loaded PVA-g-LA hydrogel films in acetone as well as the reswelling behavior of the PPH-loaded PVA-g-LA hydrogel films in water were investigated. The curing time and curing temperature condition significantly affected to the ratio of water absorption and the ratio of water retention due to the higher strength interaction of ester bond between the hydroxyl groups of PVA and the carboxyl groups of LA in their structure [6, 10].

The moisture content in the PPH-loaded PVA-g-LA hydrogel films was measured by moisture analyzer and calculated as a percentage of moisture content that are shown in Figure 2. When increased the amount of the LA, it was found that the moisture content in the PPH-loaded PVA-g-LA hydrogel films increased, but at the maximum amount of the LA mixing found the decreasing of the moisture content in the PPH-loaded PVA-g-LA hydrogel films because the higher strength interaction between of ester bond between the hydroxyl groups of PVA and the carboxyl groups of LA might be obtained.

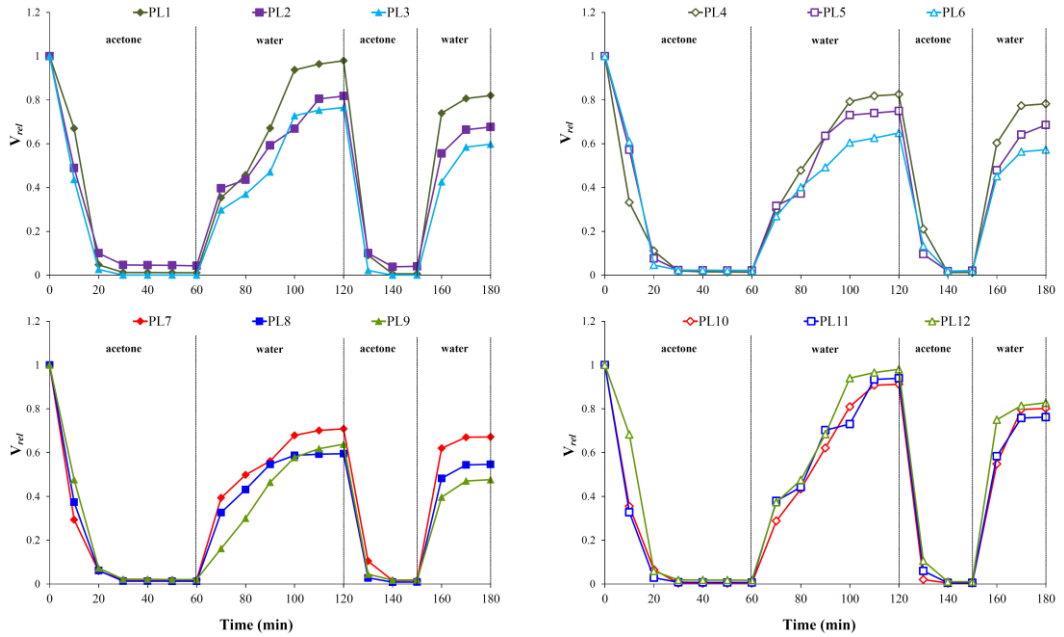


Figure 1. The swelling-deswelling behaviors of PPH-loaded PVA-g-LA hydrogel films.

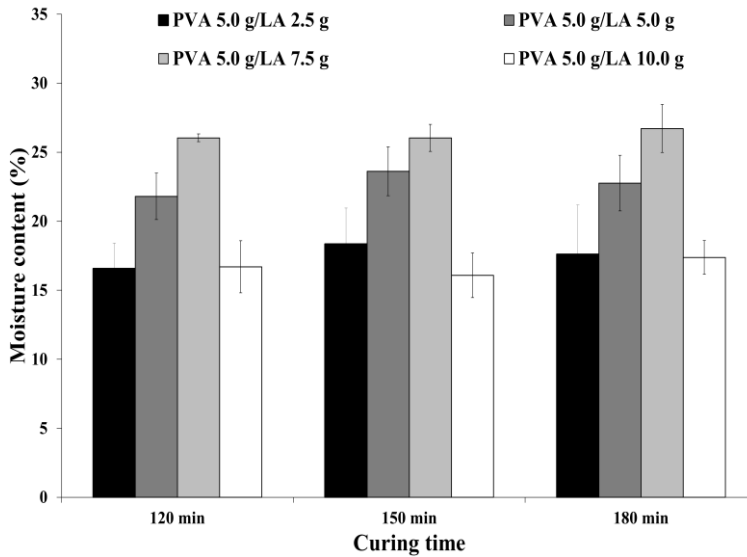


Figure 2. The moisture content of PPH-loaded PVA-g-LA hydrogel films.

The PPH-loaded PVA-g-LA hydrogel films were swollen in water at room temperature that had a value of the ratio of the water absorption at 2.20 ± 0.53 . It was clear that the latter floats in water, whereas the PPH-loaded PVA-g-LA hydrogel films was measured that are shown in Figure 3 and 4. To better understand the swelling behaviors of the PPH-loaded PVA-g-LA hydrogel films in presence of different cations, the chloride salts of Na^+ and K^+ with the concentration of 10 mmol/L were employed as swelling media. The results of the ratio of the water absorption in saline solutions was clearly decreased that comparing with distilled water as swelling media. This is due to the theoretical equilibrium swelling capacity and the initial swelling rate constant in saline solution are much lower than in distilled water that is reported [18]. Because of the additional cations causing a nonperfect anion-anion electrostatic repulsion, leading to a decreased osmotic pressure or ionic pressure

difference between the hydrogel network and the external solution [19]. The pH value is one of the most important parameters affecting the absorption process [20], thus this work studied the influence of pH values ranged from 2 to 10 on water absorption of PPH-loaded PVA-g-LA hydrogel films. It was found that the swelling behaviors were depended on pH value. When the pH value was changing in the range of 2 to 7, the swelling capacity of PPH-loaded PVA-g-LA hydrogel films increased, but decreased at pH 10. Because of the low pH value had the higher protonation degree of carboxyl groups. The carboxyl groups become ionized and the electrostatic repulsion between the molecular chains was predominated at high pH value, leading the network more expanding [21]. But the higher pH value at 10, the decreased of swelling capacity could be explained by the theoretical equilibrium swelling capacity and the initial swelling rate constant in swelling media are much lower than in distilled water that related to the above description. The theoretical equilibrium swelling capacity and the initial swelling rate constant increased as pH increasing from 2 to 6, but decreased at pH more than 8 [18].

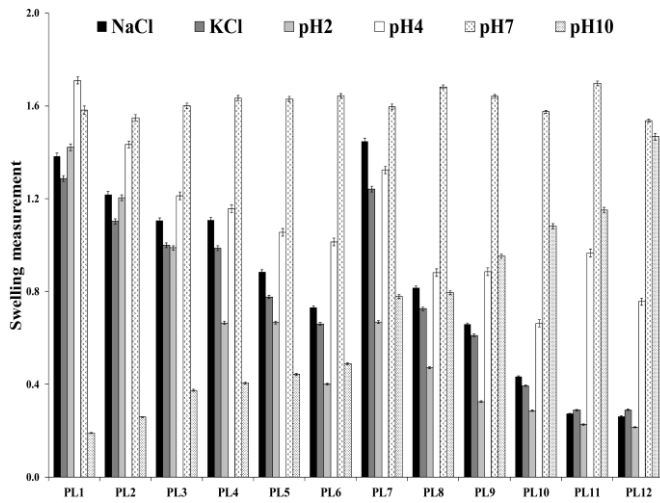


Figure 3. The swelling measurement of PPH-loaded PVA-g-LA hydrogel films in various aqueous solutions.

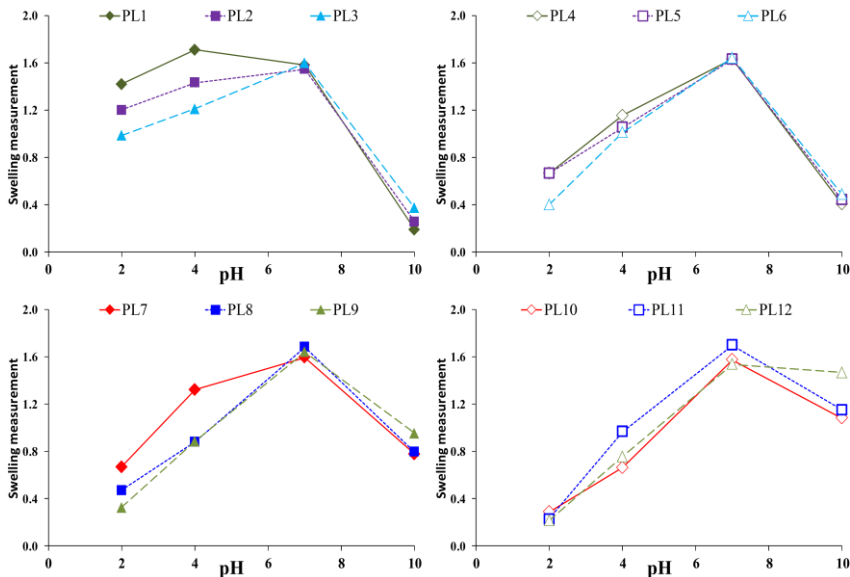


Figure 4. The swelling measurement of PPH-loaded PVA-g-LA hydrogel films in various pH conditions.

4 Conclusions

The swelling properties of PPH-loaded PVA-g-LA hydrogel films were investigated and measured. It was found that the different environmental stimuli fluids such as water, various pH, and various ionic strength and the amount of the LA were affected on swelling properties of PPH-loaded PVA-g-LA hydrogel films. The PPH-loaded PVA-g-LA hydrogel films showed the high swelling behavior in water, but rapidly deswelling behavior in acetone. The PPH-loaded PVA-g-LA hydrogel films had a high swelling in the medium pH 7. Thus, the prepared PPH-loaded PVA-g-LA hydrogel films had a good swelling property that might be used to controlled release of the drug in pharmaceutical product.

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