Effect of Crosslinking on Release of Model Drug from Electrospun Poly(vinyl alcohol) Fiber Mats

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Introduction

The electrospinning is a simple and versatile technique used to produce ultrafine fibers. The fibers produced by this technique have diameter in nanoscale. The mat of electrospun fibers has large specific surface area and fine porous structure which are benefits for the applications in drug delivery system. Although the electrospinning technique has been widely used in preparation of drug carrier, none of them had crosslinked the electrospun fibers in order to control the drug release. In this contribution, poly(vinyl alcohol), (PVA) is selected to be a carrier for deliver a non-steroidal anti-inflammatory drugs, sodium salicylate (SS) (freely soluble in water). PVA is one of the most widely used hydrogel and it is interesting here because of its biocompatibility, non-toxicity, good water permeability, and, particularly, excellent electro-spinnability.

In order to reduce the dissolution of PVA, improve the mechanical properties of SS-loaded electrospun PVA mat and control the drug release profile, after electrospinning process, the SS-loaded electrospun PVA mat was further cross-linked by glutaraldehyde vapor and glyoxal vapor. By this method, it is believed that the toxicity of the crosslinked sample is minimized.

The alternative approach to control the drug release profile from the electrospun fibers has been proposed here. The SS-loaded electrospun PVA mat was cross-linked by using glutaraldehyde vapor and glyoxal vapor. The morphology, thermal behavior, swelling behavior, release characteristic, kinetics of drug release and also toxicity of the cross-linked sample were investigated.

Experimental

A weighed amount of PVA powder was dissolved in distilled water at 80°C for 3 hr to prepare a PVA solution at a fixed concentration of 10% w/v. After the solution was cooled down to room temperature, the model drug was added into the PVA solution under constant stirring for 4 hr prior to electrospinning. Drug was loaded at 20 wt% (based on the weight of PVA powder).

Electrospinning of the as-prepared solution was carried out by connecting the emitting electrode of positive polarity from a high voltage DC power to the solutions and the grounding electrode to a rotating metal drum, used as the fiber-collecting device. The electrostatic field strength was fixed at 15 kV/15 cm. The thickness of the electrospun mats was controlled between 20 and 30 μm.

The drug-loaded electrospun PVA mats were cross-linked by separate treatment with glutaraldehyde vapor and glyoxal vapor from a saturated 5.6 M glutaraldehyde aqueous solution and glyoxal aqueous solution, respectively, at 37°C for 0 to 8 h. After treatment, the samples were further heated in vacuum oven at 40 °C for 30 h and then kept in desiccators for at least 5 days before characterization.

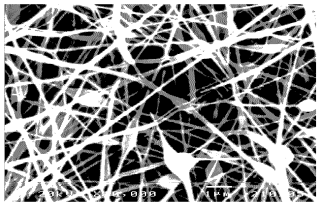

Figure 1. Selected scanning electron micrographs (10,000x) of drug-loaded as-spun PVA mats from 10% w/v PVA solutions loaded with a model drug at 20% by weight of PVA.

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Results and discussion

From Figure 1, it showed that the electrospinning of SS-containing PVA solutions resulted in the formation of beaded fibers with the average diameter was about 107.8 ± 34.8. After Cross-linking with glutaraldehyde vapor and glyoxal vapor, the morphology of the SS-loaded as-spun PVA mat was change to interconnected fiber and then densely packed as the cross-linking time increased.

The swelling test was done by immerse samples in distilled water at 37°C for 24 hr. After cross-linking, the degree of swelling and the weight loss of the SS–loaded as-spun PVA mats were lower for both types of cross-linking agents; glutaraldehyde and glyoxal vapor. In addition, the degree of swelling and the weight loss of the SS–loaded as-spun PVA mats were lower with increasing cross-linking time. There were two possible reasons for explaining the decreasing in the degree of swelling after cross-linking. Firstly, the reaction between the hydroxyl group of PVA and the aldehyde group of the cross-linking agents that leaded to connected molecular chain which reduced the swelling properties and also the dissolution property or the %weight loss. The other was due to the lower surface area of the samples after cross-linking process that resulted in decreasing of the degree of swelling.

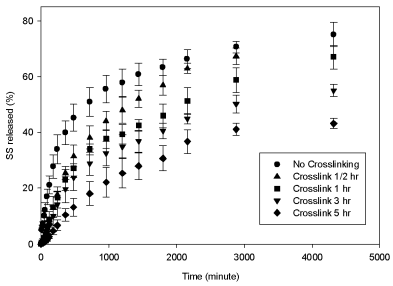

Figure 2. Profile of drug released from SS-loaded electrospun PVA mats before and after cross-linking with glutaraldehyde vapor by transdermal diffusion through a pig skin technique during 3 days.

The release characteristics of the SS from the SS-loaded as-spun PVA mats were carried out by the transdermal diffusion through a pig skin methods. The experiments were carried out using acetate buffer as the transfer medium at a controlled temperature of 37°C. The cross-linking technique by glutaraldehyde vapor and glyoxal vapor can slow down the release rate as shown in Figure 2. At the same cross-linking time, cross-linking with glutaraldehyde vapor appeared to be more effective than gloxal vapor. But both of them can slow down the rate of SS release which depended on the time used to cross-link.

The indirect cytotoxicity evaluation of cross-linked SS–loaded as-spun PVA mats was conducted using human dermal fibroblast cells. The result was obviously showed that both glutaraldehyde and glyoxal vapor can use to cross-link SS–loaded as-spun PVA mats without creating toxicity. Although the toxicity of glutaraldehyde is widely well known, its toxicity was minimized by the cross-linking technique used in this study.

Conclusions

Electrospinning of SS-containing PVA solutions resulted in the formation of beaded fibers. The SS-loaded electrospun PVA mat were cross-linked by glutaraldehyde vapor and glyoxal vapor. The results showed that after cross-linking, degree of swelling and % weight losses were decreased. The release rate of SS from SS-loaded electrospun PVA mat was reduced as the cross-linking time increased. In addition, the cross-linked SS–loaded as-spun PVA mats did not created any toxicity to the human dermal fibroblast cells.

References

[1] Peppas N A and Khare A R. *Adv. Drug Delivery Rev.***1993**, 11, 1.
[2] B. Ding, H.Y. Kim, S.C. Lee, C.L. Shao, D.R. Lee, S.J. Park, G.B. Kwag, and K.J. Choi. *J Polym Sci: Polym Phys*. **2002**, 40, 1261.
[3] Taepaiboon P, Rungsardthong U and Supaphol P *Nanotechnology* **2006**, 17(9), 2317.
[4] L.L. Wu, X.Y. Yuan, and J. Sheng. *J Membrane Sci*. **2005**, 250, 167.