# EFFECTS OF CARBON OF CARBON BLACK FOR CONTROLLED DRUG RELEASE IN ELECTRO-RESPONSIVE TRANSDERMAL DRUG RELEASE SYSTEM

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## Introduction

Transdermal delivery of drugs through the skin to the systemic circulation provides a convenient route of administration for a variety of clinical indications. The use of an electric field as an external stimulus is an efficient method that has been successfully employed to enhance the amount of released drug and the precise controls under simply controlling the applied voltage [1]. In this study, the electrically conductive and electro-sensitive transdermal delivery system (TDS) was prepared and investigated in order to solve the above problems. For the enhanced electrical conductivity, carbon black is applied as an additive. Finally, nano fiber of poly(vinyl alcohol)/carbon black/photo initiator/drug were produced, cured using ultraviolet (UV) radiation and using electrospun method.

## Experimental

Poly (vinyl alcohol) (87 ~ 89 % hydorolyzed, Aldrich) and carbon black (Korea carbon black) were used. The drug, namely ketoprofen (99% purity) was purchased from Ardrich (USA). Irgacure 2959 (Ciba chem.) is used as photo initiator. 0.1M NaOH (Samchun) solution is for Ketoprofen.

Poly (vinyl alcohol) solution was prepared by mixing 3 g of Poly (vinyl alcohol) with 30 ml of 0.1 M NaOH solution. Then, the ketoprofen powder was mixed with Poly (vinyl alcohol) solution. After make the solution, 0.005 g Irgacure 2959 was added and dissolved in the PVA solution.

A scanning electron microscope (SEM), Infrared (IR) spectra, Attenuated total reflection infrared spectroscopy (ATR-IR) instrument, and UV-vis spectro-photometer were used for analysis the sample.

Permeation experiments were conducted in vertical Franz-type diffusion cells (Disa, Milan, I). The hairless mouse membrane was mounted between the donor and receptor compartments of diffusion cells with the epithelial side facing the donor compartment. The diffusional surface area was 3.14 $cm^2$.

The schematic of TDS was depicted in Fig. 1. After an equilibration period of 30 min with PBS on both sides of the tissue, 0.2 mg of the electrospun fibers was applied on the mucosal surface in the donor compartment and 0.5 ml of PBS was then added. And the electric voltage (0, 5, 10, and 15 V) was applied. With 1 h of interval time period, sample (2ml) was withdrawn from the receiver compartment and replaced immediately with an equivalent volume of fresh PBS at 37 ± 1 ℃.

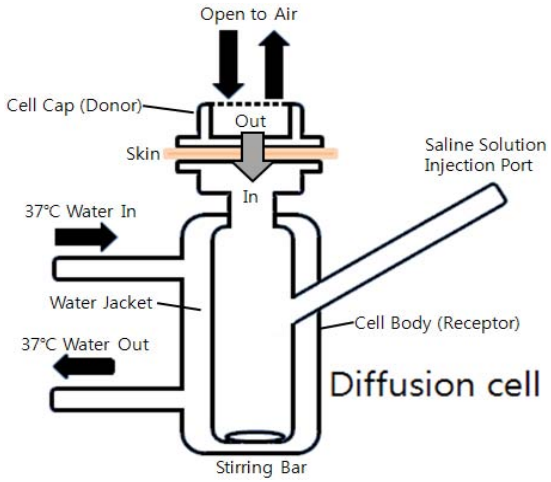


**Fig. 1** Franz diffusion cell system.

## Results and Discussion

The morphology was studied on SEM images, as shown in Fig. 2. Ketoprofen drug-loaded electrospun fiber which had not crosslinked (PF1) was formed of uniform fibers having an average diameter of 100 ± 50 nm, with smooth and clean surfaces. Beside crosslinked PVA fiber (PF2) had 200 ± 20 nm wrinkles on the surface, which resulted from the ultraviolet (UV) radiation.

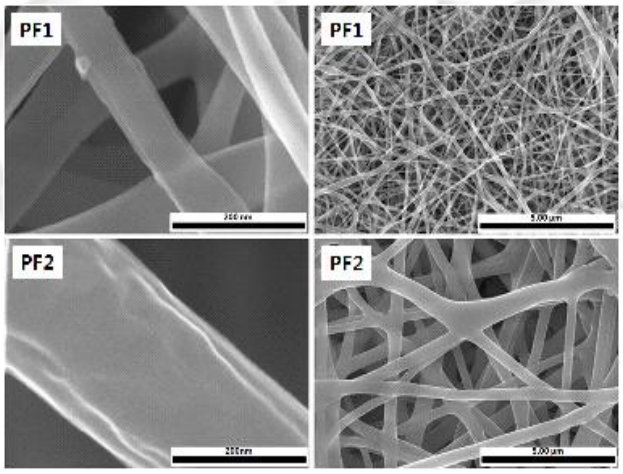


**Fig. 2** Surface morphology of PVA fiber.

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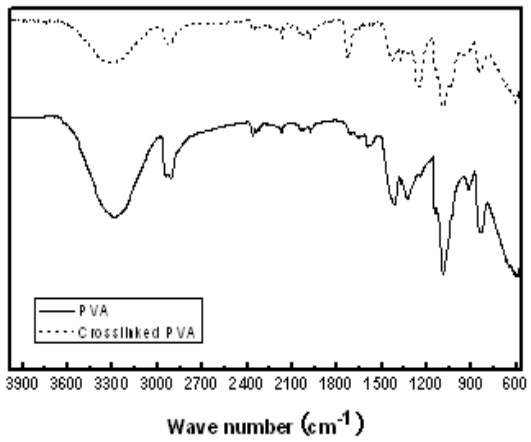


**Fig. 3** ATR peaks of pure PVA fiber and crosslinked PVA fiber.

The ATR peaks were shown in Fig. 3 in order to investigate the chemical bonds of pure PVA fiber and crosslinked PVA fiber. The sample was selected for that, to avoid the complex overlapping peaks from the drug. C=C, C-O, and C=O stretching vibrations (STR) were observed by crosslinked Irgacure 2959. C-O and O-H STRs were shown by PVA polymer. C-H STR and bend were also observed by crosslinked Irgacure 2959 and PVA polymers [2].

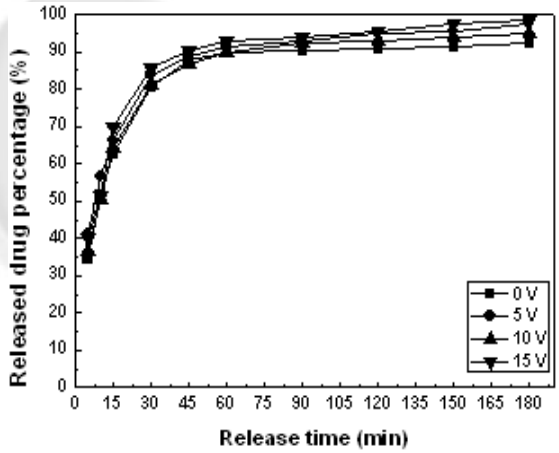


**Fig. 4** Drug release data of PF1.

The effect of the crosslinked of the electrospun PVA fibers on the release of Ketoprofen was studied using non-crosslinked sample (PF1), as shown in Fig. 4. In case of PF1, the amount of released drug increased with increasing the applied electric voltage from 90.1 ± 1.2 to 98.7 ± 1.8 % in Fig. 4. In case of PF2, the released drug amount reached almost 60 ± 3.0 % to 90.6 ± 5.0 %. It means that crosslinking method can be control the drug release.

When comparing PF1 and PF2 samples without the applied electric voltage, the PF1 showed the higher released amount of drug. It is considered that the crossliking method play as a barrier by blocking the space for releasing the drug. The UV photo polymerization is dependent upon the formation of reactive free radicals generated through the use of photo initiators, which may be classified into two main categories related to their mechanism of free radical formation: photo cleavage or photo fragmentation, and hydrogen abstraction [3]. The photo initiator chosen for this study was Irgacure 2959 which photo fragments to yield a highly reactive methyl radical. The methyl radical initiates the polymerization of a copolymer network by attacking the PVA. And then the polymerization of PVA occurred. This reaction can occur continually and PVA polymers might be stuck physically among crosslinked Irgacure 2959 polymers forming the interpenetrating polymer network (IPN) structure.

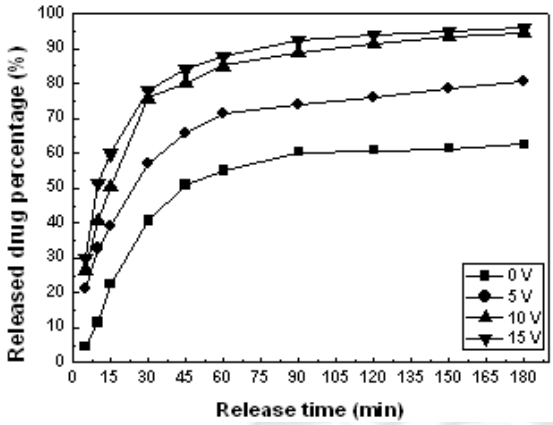


**Fig. 5** Drug release data of PF2.

## Conclusions

The electrically conductive and electro-sensitive transdermal delivery system (TDS) was prepared by electrospun method by using Poly (vinyl alcohol) and Irgacure 2959 polymers. Carbon black was embedded as a conductive additive and observed in the middle of electrospun fibers. The released drug increased under higher applied electric voltage effectively by effects of the excellent electrical conductivity of carbon additive. The mechanism of releasing the drug was suggested that Poly(vinyl alcohol) of IPN was dissolved generating the way for releasing drug affected by electric voltage.

### References

[1] Yun JM, Im JS, Jin DH, Lee YS, Kim HI. Controlled Release Behavior of Temperature Responsive Composite Hydrogel Containing Activated Carbon. Carbon Lett 2008;9(4):283-288.

[2] Juntanon K, Niamlang S, Rujiravanit R, Sirivat A, Electrically controlled release of sulfosalicylic acid from crosslinked poly(vinyl alcohol) hydrogel. Int J Pharm 2008;356(1):1-11.

[3] Mellott MB, Searcy K, Pishko MV. Release of protein from highly cross-linked hydrogels of poly(ethylene glycol) diacrylate fabricated by UV polymerization. Biomaterials 2001;22(9):929-941.