**Transdermal Delivery of Captopril Using Poly(vinyl alcohol)/Poly(N-vinyl caprolactam)-based Hydrogel-Forming Microneedle**

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**Background and aims.** Captopril (CAP) is commonly used to treat hypertension, but its low oral bioavailability and short half-life limit its efficacy [1, 2]. One strategy to overcome this problem is using transdermal hydrogel-forming microneedles (HFMN), which swells upon hydration. Previously, HFMN was fabricated using poly(vinyl alcohol) (PVA) and poly(vinyl pyrrolidone) [3]. In this research, we developed HFMN using PVA and poly(N-vinyl caprolactam) (PNVCL) for alternative transdermal delivery of CAP.

**Methods.** The hydrogel film (HF) was optimized by varying crosslinking time, also PNCVL and citric acid (crosslinking agent) concentrations. Physicochemical properties and permeability of the HF were evaluated. The most promising HF formulations were selected as HFMN materials. HFMN was fabricated using micromold (225 needles, height of 600 µm). Meanwhile, CAP-loaded film was prepared using PVP and glycerol [3]. The selected HFMN were assessed for their morphology, mechanical strength, and insertion ability. I*n vitro* permeation test using Franz diffusion cell and *in vivo* antihypertensive activity were also conducted. The analytical method for quantifying CAP was validated as per International Council for Harmonisation guidelines [4].

**Results.** Cumulative amount of CAP permeated through the PVA/PNVCL-based HF was >40%. The most optimum crosslinking time and citric acid concentration were 45 minutes and 1.0% w/w, respectively. Furthermore, the addition of PNVCL (10% w/w) increased the mechanical properties of the HFMN. The most promising HFMN formulation for enhancing transdermal delivery of CAP out of 6 formulations was F3, with a cumulative amount of drug permeated of 13.59 ± 2.54 mg (~66.68 ± 2.78%). The *in vivo* study confirmed that transdermal delivery of CAP using HFMN was more effective than the oral group, especially in lowering blood pressure, and there were no signs of redness or irritation observed on the rat skin.

**Conclusion/Discussion.** We have successfully optimized and fabricated PVA/PNVCL-based HFMN for transdermal delivery of CAP.

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