

Pengembangan Hydrogel-Forming Microneedles Berbasis Poli(Vinil Alkohol) Dan Poli(N-Vinil Kaprolaktam) dengan Perbedaan Agen Penaut Silang untuk Penghantaran Kaptopril Secara Transdermal = Development of Hydrogel-Forming Microneedles Based on Poly(Vinyl Alcohol) and Poly(N-Vinyl Caprolactam) with Different Crosslinking Agent for Transdermal Delivery of Captopril

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Abstrak

Kaptopril merupakan antihipertensi lini pertama pada terapi hipertensi. Pemberian kaptopril melalui rute oral memiliki kekurangan, seperti frekuensi pemberian yang cukup tinggi, bioavailabilitas yang rendah akibat makanan, dan pasien yang memiliki kesulitan menelan. Penghantaran kaptopril secara transdermal dapat mengatasi masalah ini. Kaptopril bersifat hidrofilik dan sulit untuk melewati stratum korneum, maka dikembangkan Hydrogel-forming Microneedles (HFMN). Tujuan dari penelitian ini adalah untuk memformulasikan dan mengevaluasi HFMN berbasis poli(vinil alkohol) (PVA) dengan kombinasi poli(N-vinil kaprolaktam) (PNVCL) atau poli(vinil pirolidon) (PVP) yang terintegrasi dalam film untuk penghantaran kaptopril secara transdermal. Sebelum memformulasikan HFMN, dilakukan formulasi film hidrogel untuk menghasilkan film hidrogel yang optimal untuk menghantarkan kaptopril, meliputi evaluasi fisik, fisikokimia, kemampuan swelling, dan permeabilitas. Formula film hidrogel terpilih akan dikembangkan menjadi HFMN dan dievaluasi secara fisik, kemampuan swelling, permeabilitas, insersi, dan kekuatan mekaniknya. Film hidrogel yang dibuat dapat mengembang hingga $252,42 \pm 5,65\%$ selama 24 jam dan memfasilitasi difusi kaptopril sebesar $52,76 \pm 0,53\%$ setelah 24 jam. Formula HFMN optimal yang akan diintegrasikan dengan reservoir film kaptopril adalah F2 (10% PVP, 1,5% asam malat) dan F3 (10% PVP, 1,5% asam suksinat). HFMN yang dibuat memiliki kemampuan swelling hingga $190,73 \pm 2,04\%$ selama 1 jam serta mampu menembus lapisan Parafilm® M hingga kedalaman 500 m dengan pengurangan tinggi jarum sebesar $8,92 \pm 1,19\%$. Pada uji permeasi in vitro, persentase obat kumulatif selama 24 jam dari HFMN terintegrasi film kaptopril adalah F2 ($44,94 \pm 21,48\%$), F3 ($33,88 \pm 14,13\%$), dan F4 ($28,12 \pm 0,18\%$) dan berbeda signifikan secara statistika (p-value 0,0003). F2 berbeda signifikan terhadap F3 (p-value 0,0026) dan F4 (p-value 0,0003). Hasil penelitian ini menunjukkan pengembangan HFMN dengan perbedaan agen taut silang dan polimer mempengaruhi permeasi dari obat dan kemampuan swelling.

.....Captopril is an antihypertensive drug which is the first line therapy for hypertension. However, giving captopril via the oral route has disadvantages, such that high frequency of administration per day, low bioavailability due to food, and patients who have difficulty swallowing. Nevertheless, transdermal delivery of captopril can overcome this problem. Furthermore, captopril is hydrophilic and difficult to pass through the stratum corneum. So, hydrogel-forming microneedles (HFMN) were developed. The aim of this study was to formulate and evaluate poly(vinyl alcohol) PVA-based HFMN with a combination of poly(N-vinyl caprolactam) (PNVCL) or poly(vinyl pyrrolidon) (PVP) integrated with film for transdermal delivery of captopril. Before formulating HFMN, hydrogel film formulation was carried out to produce an optimal hydrogel film to deliver captopril, which were evaluated their physical characteristics, physicochemistry, swelling ability, and permeability. HFMN was made and evaluated for its physical, swelling ability,

permeability, insertion and mechanical strength. The hydrogel film created was able to swell up to $252.42 \pm 5.65\%$ within 24 hours and facilitate the diffusion of captopril by $52.76 \pm 0.53\%$ after 24 hours. The selected hydrogel films that was developed into HFMN were F2 (10% PVP, 1.5% malic acid), F3 (10% PVP, 1.5% succinic acid), and F4 (2.5% PNVCL, 1.5% citric acid). The HFMN chosen for delivering captopril with a captopril film reservoir were F2 (10% PVP, 1.5% malic acid) and F3 (10% PVP, 1.5% succinic acid). The fabricated HFMN was able to swell up to $190.73 \pm 2.04\%$ within 1 hour and penetrate the Parafilm® M layer to a depth of 500 μm with a reduction in needle height of $8.92 \pm 1.19\%$. In the in vitro permeation test, the cumulative percentage of captopril that permeated from the HFMN integrated captopril film for each formulation was $44.94 \pm 21.48\%$ (F2), $33.88 \pm 14.13\%$ (F3), and $28.12 \pm 0.18\%$ (F4), with significant difference (p-value 0.0003) among the tested formulations. F2 was significantly different from F3 (p-value 0.0026) and F4 (p-value 0.0003). The results of this research showed that the development of HFMNs with different crosslinking agents and polymers affected the permeation of drugs and swelling ability.