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THE INFLUENCE OF OLEIC ACID AND PROPYLENE GLYCOL ON LOSARTAN TRANSDERMAL TRANSPORT *IN VITRO*

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ABSTRACT

Losartan, an angiotensin II type 1 receptor antagonist is important in hypertension therapy. The low oral bioavailability, due to intensive first pass metabolism and degradation by normal flora in the gut, requires an alternative route of delivery, with transdermal route as an attractive candidate. Nonetheless, there is limited number of studies in this topic. Therefore, this study was aimed to characterize the transport of losartan as well as to optimize the transport based on the presence of propylene glycol and oleic acid as enhancer. Studies were carried out in a vertical diffusion cells where the fresh rat skin was mounted in between the donor and acceptor compartments. Propylene glycol (PG) was incorporated into drug donor solution, while oleic acid (OA) was introduced as an enhancer pretreatment to rat skin prior to the transport studies. Factorial design method was implemented to estimate the optimum formulation condition based on the transport data parameters, i.e. steady state flux ($Flux_{ss}$) and diffusion lag time (T_{lag}),. Factors studied in the design were drug donor concentration, PG donor concentration and duration of OA pretreatment to the skin. Losartan transpor was optimum at high level of drug donor concentration, low level of PG donor concentration and longer duration of OA pretreatment. Based on the maximum $Flux_{ss}$ achieved (23.1 µg/cm^2/h), the estimated plasma concentration of losartan could reach a level of 0.1 µg/ml, which indicates the feasibility of transdermal delivery of losartan. This however requires a solution of the long T_{lag} (15h) during the transdermal transport.