

THE EFFECTIVENESS OF DERMAROLLERS® IN IMPROVING TRANSDERMAL DELIVERY OF PRIMAQUIN IN THERMORESPONSIVE-BIOADHESIVE HYDROGEL FORMULATIONS

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Background: Malaria has affected 228 million people in world. Oral administration of primaquine (PMQ) has been applied as a conventional treatment for this infection disease. Nevertheless, numerous drawbacks were reported associated with this conventional therapy. Therefore, the development of new delivery approach is urgently needed. Here, for the first time, PMQ was incorporated into thermoresponsive-mucoadhesive hydrogels for improved and sustained transdermal delivery of PMQ combined with Dermarollers®.

Methods: Thermoresponsive-bioadhesive hydrogels were formulated using Pluronic F127 (PF127) and Pluronic F68 (PF68) as thermosensitive polymers and HPMC as bioadhesive polymer. The hydrogels contained 1% w/v PMQ. The formulations were then evaluated for their gelation temperature, bioadhesive properties, *in vitro* release and *ex vivo* permeation behaviours. Finally, the skin permeability of PMQ from thermoresponsive hydrogels was investigate *ex vivo* with the use of Dermaroller®.

Results: After various formulation optimizations, formulation containing 15% PF127, 3% PF68 and 0.4% HPMC with 1% PMQ was considered as the optimum formulation. The optimized formulation possessed desired thermoresponsive and bioadhesive properties. Importantly, the use of HPMC as bioadhesive agent did not change thermoresponsive characteristic of the formulation. The formulation showed gelation temperature at the skin temperature (32°C) with shear thinning behavior. *In vitro* release study showed biphasic release manner of PMQ from the hydrogel over 24 h. Essentially, in *ex vivo* permeation study, Dermaroller® with the length of 1 mm was able to improve and sustain the permeability of PMQ through rats' skin by 4-fold compared to untreated skin over 72 h experiments. Following these interesting studies, the efficacy of PMQ from this approach should be evaluated in *in vivo* studies.

Conclusions: Thermoresponsive with bioadhesive properties containing PMQ was successfully developed using PF127, PF68 and HPMC. The formulation possessed an adequate thermoresponsive and bioadhesive characteristic, as well as *in vitro* biphasic release manner. Importantly, Dermaroller® was able to increase and sustain the permeation of PMQ through rats' skin.